VOLUME 8 NUMBER 4

ARCHIVES OF

NEUROLOGY AND PSYCHIATRY

OCTOBER, 1922

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $6.00

Entered as second-class matter, Jan. 7, 1919, at the postoffice at Chicago, Illinois, under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized Jan. 15, 1919.

CONTENTS OF PREVIOUS NUMBERS

AUGUST, 1922 NUMBER 2

SEPTEMBER, 1922 NUMBER 3

Archives of Neurology and Psychiatry

Vol. 8 OCTOBER, 1922 No. 4

EFFECTS OF ANTISYPHILITIC THERAPY AS INDICATED BY THE HISTOLOGIC STUDY OF THE CEREBRAL CORTEX IN CASES OF GENERAL PARESIS

A COMPARATIVE STUDY OF FORTY-TWO CASES *

H. C. SOLOMON, M.D.

BOSTON

Instructor in Psychiatry and Neuropathology, Harvard Medical School; Chief of Therapeutic Research, Boston Psychopathic Hospital

AND

A. E. TAFT, M.D.

PHILADELPHIA

METHODS OF INVESTIGATION

The problem in this investigation was to determine whether any changes due to antisyphilitic treatment can be observed by histologic methods. Clinical studies have given rise to considerable divergence of opinion as to the results of antisyphilitic treatment in patients with general paresis. On the one hand there is a group of clinicians who have reported what to them have seemed satisfactory results in the treatment of paretic patients. In contrast there is probably an equally large group of clinicians who feel that the results obtained are insignificant, and there are even some who believe that the patient is made worse by the administration of antisyphilitic drugs. On theoretic grounds, likewise, there are two antipathic points of view. It has been pointed out by Spielmeyer,[1] for example, that most of the pathologic changes which occur in paresis are capable of being influenced from without or by extraneous measures. Thus, theoretically, meningitis and perivascular infiltration can be reduced, the spirochetes killed, and with the cessation of toxin formation, degenerative changes may be halted; following this, clearing up of the cellular debris, and an

* From the Neuropathological Laboratory of the Boston Psychopathic Hospital.

* This study was greatly aided by funds granted by the United States Interdepartmental Social Hygiene Board.

* Read at the Forty-Eighth Annual Meeting of the American Neurological Association, Washington, D. C., May, 1922.

1. Spielmeyer: Paralyse; Tabes; Schlafkrankheit, Ergebn. d. Neurol. u. Psychiat. **1**:217, 1911.

improvement in the pathologic picture may result. A contrary theoretical attitude championed by Noguchi and Moore points out that the spirochetes are probably in the deep tissue of the cortex at some distance from the vascular supply, that antisyphilitic drugs are on the whole prevented by a filtering process from reaching the central nervous system, and that they do not penetrate to spirochetes in the deeper

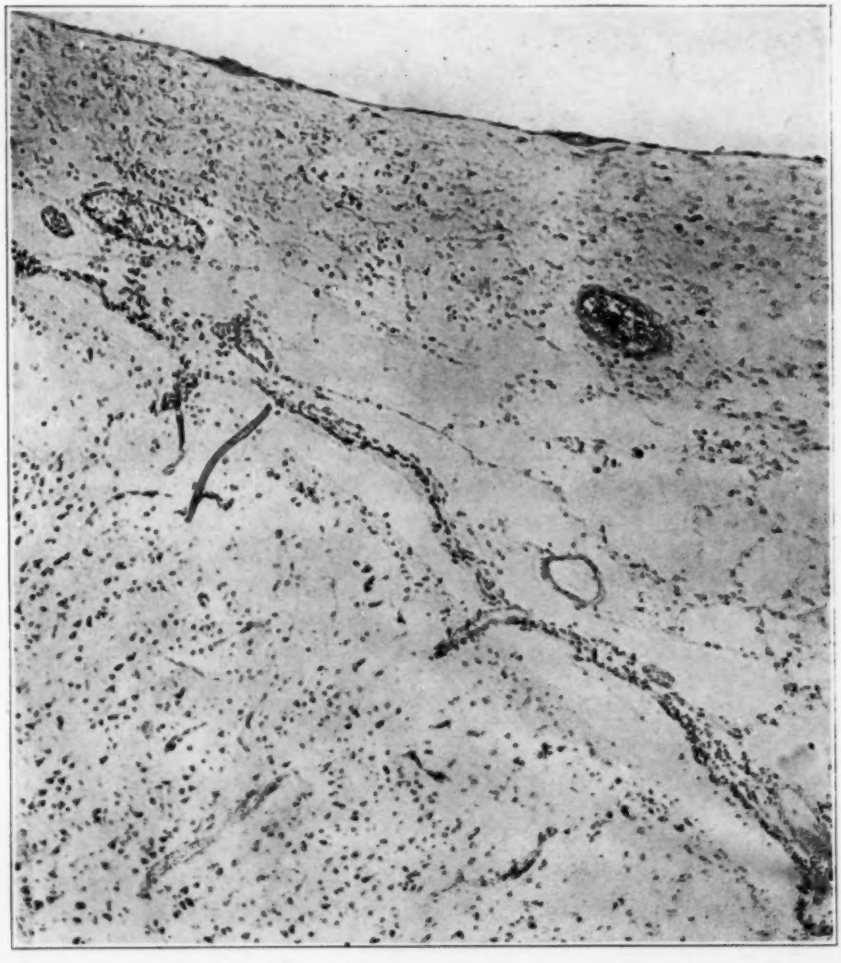

Fig. 1.—Cellular nodules in outer layer of the arachnoid; also pial edema.

situations and therefore do not accomplish any noteworthy therapeutic effect. There is, therefore, no agreement, either as to the facts or the theory, concerning the value or the possibilities of antisyphilitic treatment in cases of general paresis.

In order to determine whether there was any evidence of change in the histologic structure resulting from treatment in cases of general

paresis, a series of brains from paretic patients who had received treatment were studied in comparison with a group of brains from untreated paretic patients. The material selected consisted of brains of patients, diagnosed as having general paresis, who died in one of the Massachusetts state hospitals. It is necessary to mention that the treated

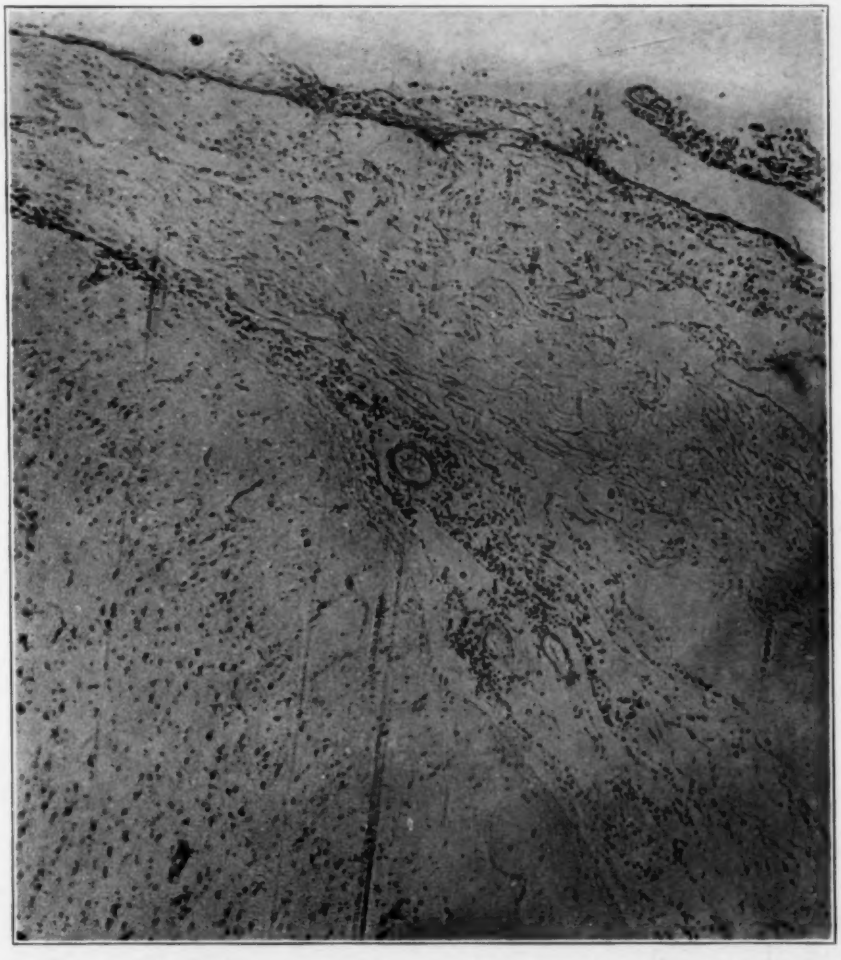

Fig. 2.—Pial edema; also characteristic type of cell infiltration, confined mainly to the pial membrane.

patients in this series did poorly from a clinical point of view, that is, they succumbed to the disease. Consequently, any changes which occur in these cases as a probable result of treatment may be expected to occur in an even greater degree in cases in which the clinical course is more favorably influenced by therapy. Blocks of tissue from brains

hardened in liquor formaldehydi were taken from the following areas of the cortex of both hemispheres of the brain: upper precentral lobe, upper postcentral lobe, tip of the temporal lobe, posterior two thirds of the first temporal gyrus, angular gyrus, calcarine cortex, cornu ammonis,

Fig. 3.—Section from central cortex; no perivascular infiltration.

base of the second frontal lobe, prefrontal lobe, Broca's area and areas of special interest. Paraffin was used chiefly in embedding, although celloidin and freezing methods were used when special stains required such methods. The stains employed were: cresyl echt violett to show

cell changes and cellular infiltration; Mallory's phosphotungstic acid hematoxylin for study of meningeal, vascular, and glial changes; Weigert's myelin sheath stain for nerve fiber study; either Marchi or sharlach R to demonstrate the presence of fat. Bielschowsky's stain for nerve fibrils was used on a few sections, but the findings did not seem of sufficient value to continue this method at length.

The cases studied were divided into two series: (1) twenty-seven patients with general paresis who had received antisyphilitic treatment in an attempt to modify the paretic process, and (2) fifteen patients with general paresis who had received no antisyphilitic treatment after the onset of psychotic symptoms. An attempt was made to study and chart in a scale the degree of intensity of the pathologic changes with reference to pial edema, pial infiltration, marginal gliosis, ameboid glial reactions, reaction of the glial cells with round nuclei, rod cell reaction, nerve cell changes, increased vascularity, vascular thickening, endarteritis, perivascular infiltration of lymphocytes and plasma cells, perivascular gummas and external hemmorrhagic pachymeningitis.

HISTOLOGIC STRUCTURE

In general, the histologic findings agree with those described by Nissl [2] and Alzheimer [3] as characteristic of general paresis. An internal hemmorrhagic pachymeningitis of long standing existed in four of the forty-two cases. This proportion is relatively small as compared with the frequency described by Wernicke,[4] Kraepelin,[5] and Bleuler.[6] Ziehen found it present in nearly one half of his cases.

The pia mater is almost always involved. Edema was present in some degree in every case. According to Alzheimer, no case of general paresis exists without pial changes. In this material the meningeal cellular infiltrate seemed to be confined mainly to the pial layer of the meninges, particularly in the vicinity of the blood vessels (Figs. 1 and 2).

The question of nerve cell changes seems well expressed by Nissl when he says that considering the prompt reaction of nerve cells to all possible injurious agencies, one cannot wonder at the variety of nerve cell changes and the importance of differentiating those found in general paresis from those in other diseases. Death in general paresis seldom occurs without some complicating terminal infection

2. Nissl: Zur Histopathologie der paralytischen Rinderkrankung, Nissl histologische und histopathologische Arbeiten **1**:315, 1904.

3. Alzheimer: Histologische Studien zur Differentialdiagnose der progressiven Paralyse, Nissl histologische und histopathologische Arbeiten **1**:18, 1904.

4. Wernicke: Grundriss der Psychiatrie, Ed. 2. Leipzig, Thieme, 1906.

5. Kraepelin: Lehrbuch der Psychiatrie, Leipzig, Barth, 1910.

6. Bleuler: Lehrbuch der Psychiatrie, Ed. 2. Berlin, Springer, 1918.

such as pneumonia, decubitis, etc. More than one half of the patients of this series died of acute terminal infections. This would seem to interfere with any possible conclusions concerning the cellular reaction in treated and untreated patients, especially with regard to the presence of fat in the cells of the cortex. For this reason, as well as for the fact

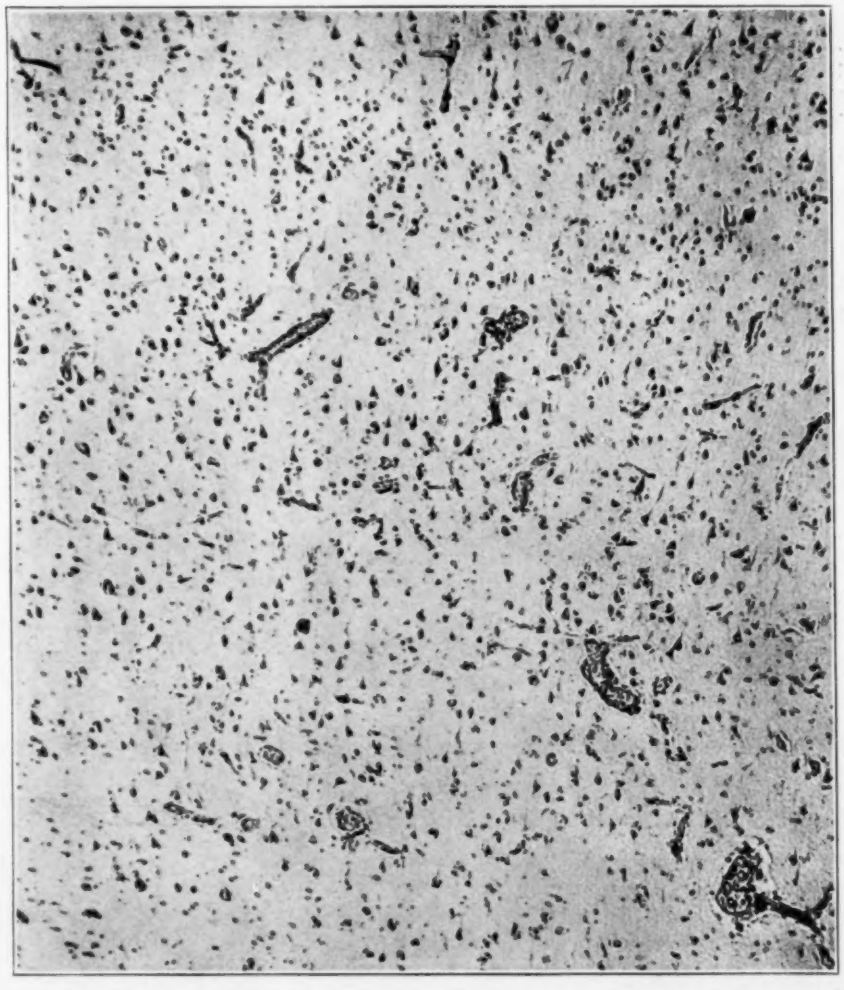

Fig. 4—From same case as Fig. 3. Temporal lobe. Note characteristic sheath infiltration of capillaries and arterioles.

that it is quite difficult to estimate the extent or degree of cell loss of one case in comparison to another, no conclusions concerning cell changes are attempted. Bielschowsky's stain for nerve fibrils shows no specific changes of significance. This has also been shown by Spielmeyer.

The neuroglia is apparently always increased in general paresis. This, of course, is a general statement. In the cases of this series there was some increase in the marginal glia fibers with the usual focal increase of astrocytes in the outer cortical layer, and frequently long fibers extended from the margin well down into the cell layers. This last was never more than moderate in degree.

Satellite cells were found in smaller proportion than is often seen in conditions other than paresis. Ameboid glia cells were found frequently in varying numbers. They were most numerous in the presence of frank tissue degeneration; otherwise, their variation seemed to depend on the presence or absence of acute infective processes. This was not constant, however, as they were found in cases without a history of terminal infection. The ameboid glia was limited almost exclusively to the white substance except when in relation to an area of degeneration, in which case it usually was accompanied by an increase in rod cells of various forms and small round glia cells. It is often noticeable that the white substance may contain enormous numbers of all these types of cells while the cortical portion is almost free from them. The reverse condition did not appear.

Vascular changes are usually emphasized in descriptions of paresis. Mott has said that the endarterium is affected in all cases. Alzheimer speaks of endothelial swelling. Ziehen rarely finds them present. Bleuler mentions atheroma; Kraepelin also found endothelial thickening. In this series the most frequent change was a general thickening of the media, often fibrous, with no demonstrable changes in the intima. This was true of vessels of all sizes, and the increase of the thickness of capillary walls was noticeable. Capillary hyperplasia was relatively infrequent and only of moderate degree. No significant differences in the vessels were noted in treated and untreated patients.

In the changes mentioned there is nothing diagnostic of general paresis although these changes are never lacking in this condition. The determining factor, histologically, is the presence of perivascular infiltration of plasma cells, the latter usually accompanied by lymphocytes. The manner in which the plasma cells surround the vessels is worthy of note in that it is a true adventitial infiltration, resulting in the formation of a sheath about the muscular portion of the vessel wall rather than merely in a collecting of plasma cells in the perivascular space. According to Nissl, both the lymphocytic and plasma cells are hematogenous, and he considers the plasma cell a transition form of the lymphocyte.

Because of the diagnostic value of the plasma cell infiltration in general paresis, much thought has been given to the possible significance of both plasma cells and lymphocytes in this disease. Alzheimer, in his

1912 "Paralysereferat," has insisted on the importance of the plasma cell in the histologic diagnosis of paresis; when plasma cells are diffusely present the diagnosis of paresis is probable, while in their absence this diagnosis can hardly be made. Both plasma cells and lymphocytes are

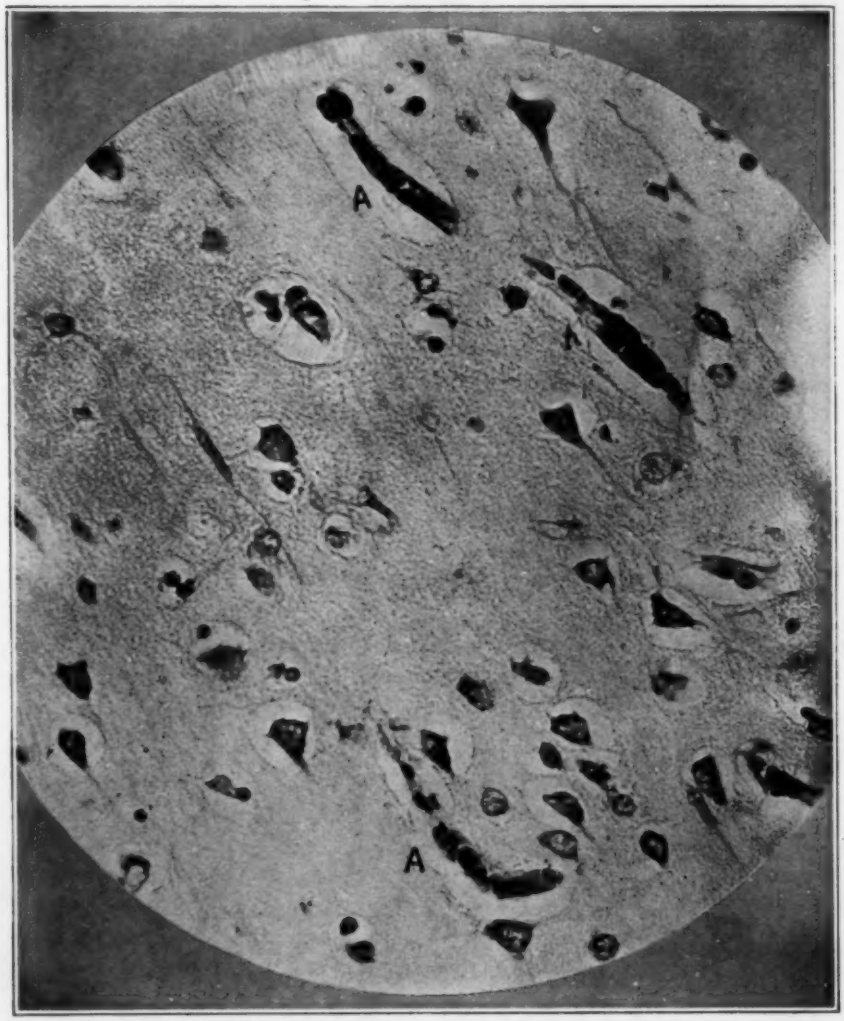

Fig. 5.—Capillaries (*A*) with plasma cells closely applied to their walls. (Untreated case.)

inflammatory cells, but whether they precede, follow or occur simultaneously with the parenchymal changes has never been determined. If the occurrence of infiltrating cells is a direct response to the toxin formation of those spirochetes which lie in close relation to the blood

vessels, the effect of antisyphilitic treatment may be different than if these perivascular cells arise in response to the irritation caused by the destruction of parenchymatous tissue; for if the latter assumption is correct, the perivascular reaction may continue even after most of the

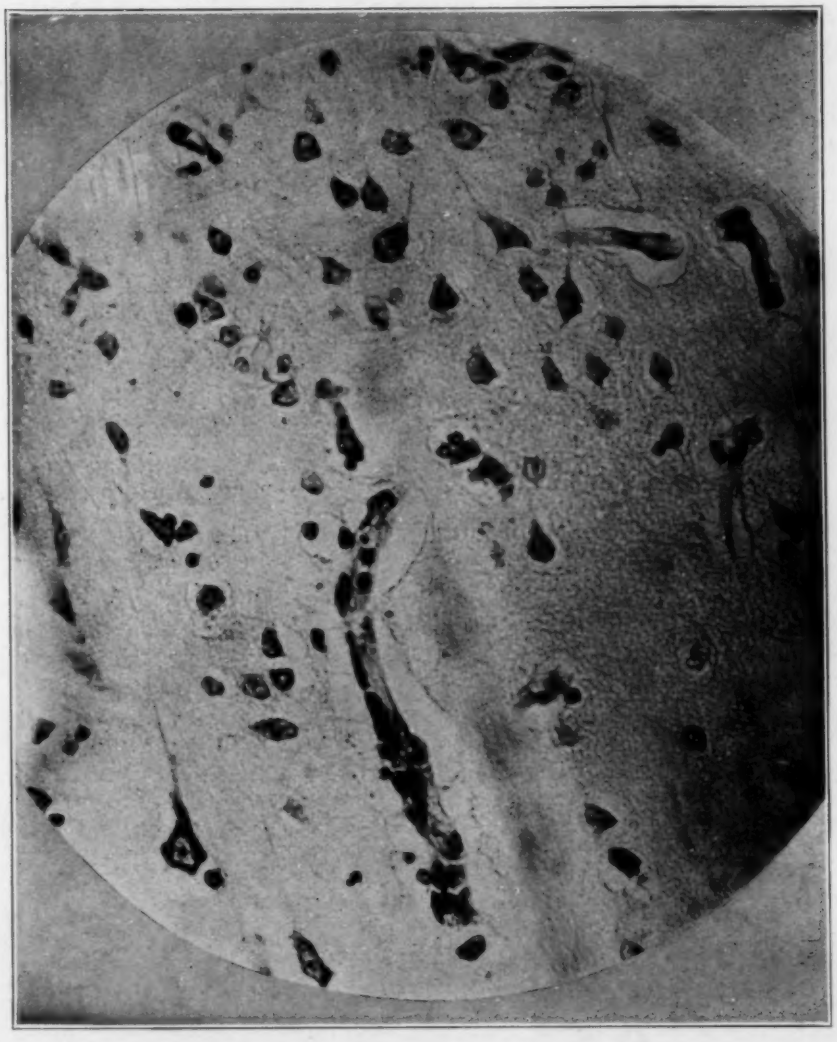

Fig. 6.—Same as Figure 5; untreated case.

organisms lying in close proximity to the vessels have been destroyed, owing to the continued destructive action on the parenchyma of a few spirochetes situated more deeply. At all events, the presence of plasma cells is known to be an evidence of chronicity, and must be considered to have this significance in paresis.

Gruner [7] discusses plasma cells at length and calls them "irritation" cells—a functional state of any lymphoid cell—and says that they revert to the lymphoid state after the stimulus of irritation has ceased.

Nägeli's [8] idea of plasma cells agrees in the main with the foregoing. He says that they are present in infections and irritations. They are found in connection with lymphocytosis but never in leukcocytosis of marrow origin. Nägeli considers lymphocytes as lipoid antigens, finding them increased in post-toxic states and various other conditions. Gruner feels that little is known of the function of the lymphocyte but agrees that any infection of lipoid character attracts them.

There seems to be no fixed rule governing the area in which the greatest degree of perivascular change may be found, but the findings in our series seemed to be most extreme the nearer one approached the base of the brain. This is especially well illustrated by one case in which the sections from the convexity were of such normal appearance as to suggest that the diagnosis of paresis was not possible. Those near the base, however, presented a perivascular plasmacytosis of marked degree (Figs. 3 and 4).

From what has been said it becomes evident that in making any comparative studies it is necessary to have sections from many areas of the cortex; this was attempted in the present study.

FINDINGS IN THIS INVESTIGATION

Our greatest interest, a comparison of the histologic findings in treated and untreated patients, revolves around the lymphocytic and plasma cell reactions in the pia and about the blood vessels of the cortex for these reasons:

1. They are the most easily compared. 2. The plasma cells are of prime diagnostic importance in general paresis. 3. Inflammatory reactions of the pia and the perivascular region are theoretically amenable to influence by drugs (for example cerebrospinal syphilis). 4. Definite differences between the two groups of cases were found in our series.

Plasma cells were present in all patients, both treated and untreated. The treated cases could nevertheless be distinguished in the majority of instances by the smaller number of plasma cells present. Lymphocytes were frequently present in treated cases and usually in a relatively greater number as compared with the plasma cells. This held true of all cases, except in the presence of definite tissue degeneration in the

7. Gruner: Biology of Blood Cells, New York, William Wood & Co., 1914.
8. Nägeli: Blutkrankheiten und Blutdiagnostik, Berlin und Leipzig, Gruyler, 1919.

form of miliary or perivascular gummas. In this instance treatment seemed to produce no perceptible change. The importance of Nissl's statement that the presence of plasma cells about the capillaries is the most significant finding in general paresis is well borne out here. The characteristic pericapillary arrangement of plasma cells in the sections

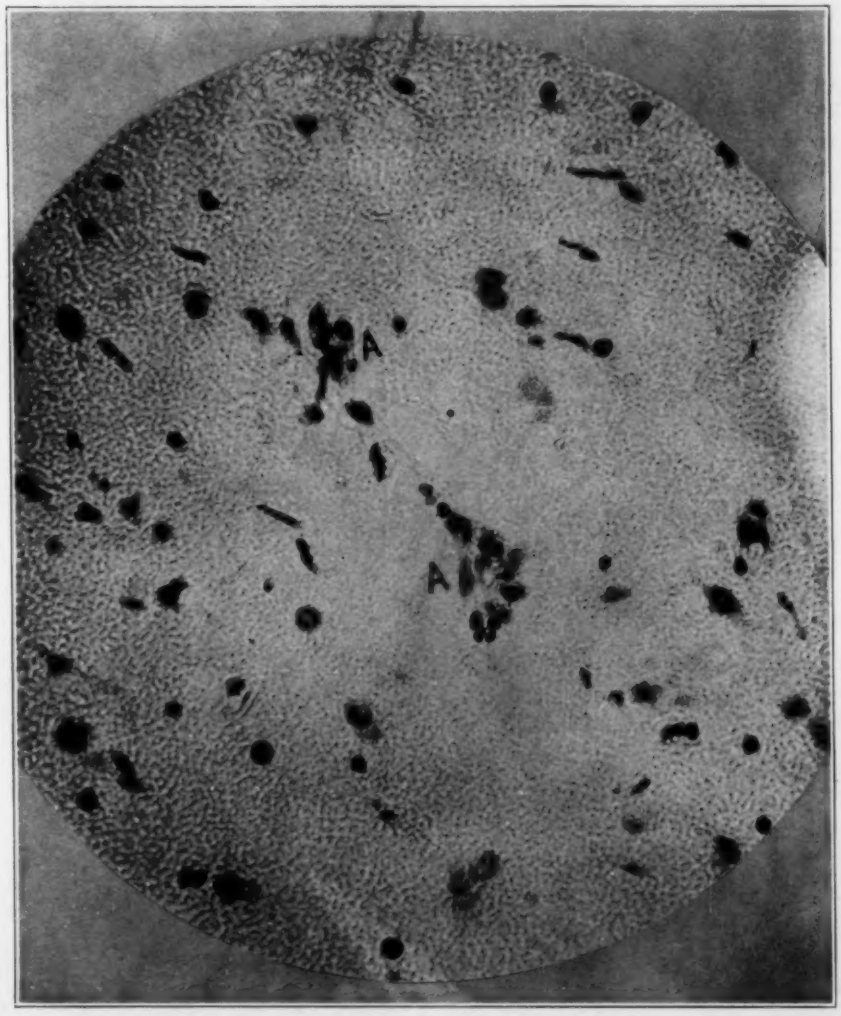

Fig. 7.—Capillaries (a). Compare with Figures 5 and 6. This patient received treatment.

from cases without treatment (Figs. 5 and 6) contrasts sharply with the absence of plasma cells in the perivascular spaces or in their occasional presence either accompanied or unaccompanied by a small number of lymphocytes in treated cases (Fig. 7).

Table 1 gives a comparison of the perivascular plasma cell, lymphocytic and pial infiltration in treated and untreated patients. The amount of infiltration is recorded as slight, moderate or considerable. Slight infiltration indicates that in no part of the various areas of the cortex examined was there more than an occasional infiltrating cell present. Considerable infiltration was credited to those cases in which the infiltration was really extensive. The others were considered as showing moderate infiltration. It will be noted that there are marked differences in the degree of plasma cell infiltration in the brains of treated and untreated patients. Thus, of the treated series of twenty-seven patients, the brains of sixteen, or more than one-half, showed slight plasma cell infiltration, whereas of the fifteen untreated patients none showed so slight a degree of plasma cell reaction. This is a difference which seems to be sharp and clear cut. Six of the treated patients, or less than one fourth, showed a moderate lymphocytosis as compared to five, or one third, of the untreated series; while five, or less than one fifth of the treated patients, showed a considerable plasmacytic reaction as compared to ten or two thirds of the untreated cases.

TABLE 1.—Comparison of Infiltration in Treated and Untreated Cases

	Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Treated	16	6	5	12	10	5	9	7	3
Untreated	0	5	10	0	9	6	1	7	4

Similar findings, although not quite so striking, are shown as regards the perivascular lymphocytic infiltration. Twelve, or almost one half of the brains of the treated patients showed a slight lymphocytic infiltration, whereas in none of those untreated was the infiltration of such minor degree. Ten, or a little less than one third of the treated patients, presented a moderate lymphocytic infiltration as compared to nine, or almost two thirds of the untreated ones; and of the treated patients only five, or less than one fifth, as contrasted with six, or more than one third of the untreated brains, showed considerable lymphocytic infiltration.

A number of the brains had had the pia stripped before this study was undertaken. However, there were nineteen brains of treated patients and twelve of the untreated ones with the pia intact. Among the treated cases nine, or practically one half of those studied for pial reaction, showed a slight pial cellular reaction as compared with one, or one twelfth, of the untreated cases. These results are given in graphic form in Fig. 8. Fig. 9 is a graphic representation of the relative proportions of the perivascular plasma cell and lymphocytic infiltration and pial infiltration, in the treated and untreated patients, by the employment

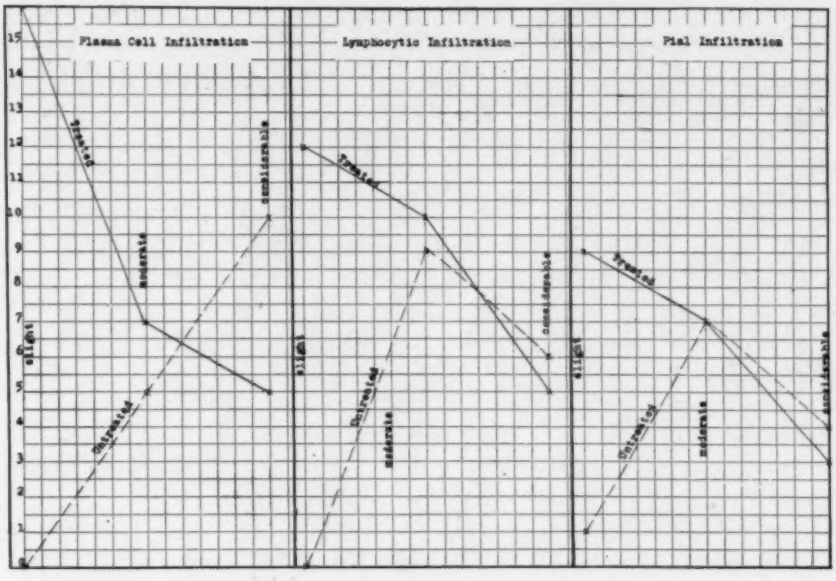

Fig. 8.—Histologic findings in treated and untreated patients with general paresis.

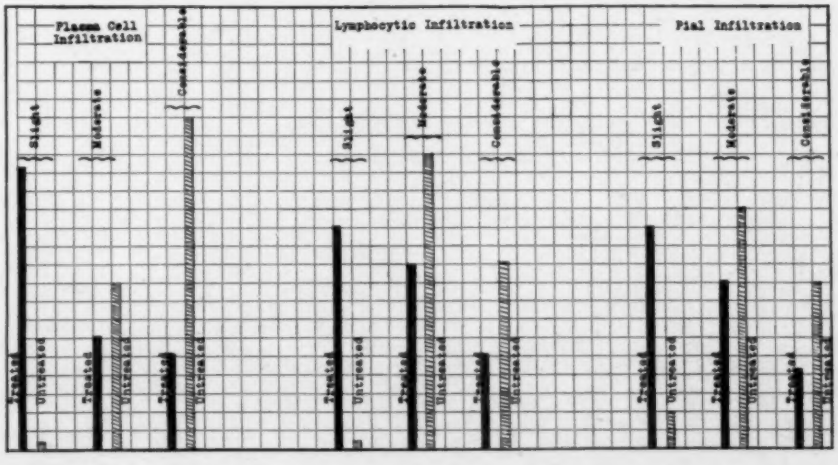

Fig. 9.—Histologic findings in treated and untreated patients with general paresis. These are charted to show relative proportions by using common denominators for the two series of cases.

TABLE 2.—Infiltration in Treated Patients Arranged in Order of Amount of Treatment Received

		Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Amount of Treatment	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Dal.	60	..	+	..	..	+	..	..	..	..
Un.	50 (5 vent.)	+	..	..	+	.	..	..	..	..
Cah.	41	+	..	..	+	..	..	..	..	..
Rey.	37 (2 sp.)	+	..	..	..	+	..	..	..	..
Hal.	31 (2 vent.)	..	+	..	+	..	..	+	..	.
O'B.	27 (5 sp.)	+	..	..	..	+	..	..	+	..
Smy.	22	..	..	+	..	+	..	..	..	+
Lar.	21	+	..	..	+	.	.	+	..	..
Per.	21	..	+	..	..	+	..	..	..	..
Hay.	21	.	..	+	..	..	+	+	+	+
Gal.	20 (2 vent., 4 sp.)	..	+	..	..	..	+	..	..	..
Mor.	20+	..	..	+	..	+	..	..	..	+
Bren.	19	+	..	..	+	..	..	+	..	..
Tho.	16	..	+	..	..	+	..	..	..	..
Ken.	15	+	..	..	+	..	..	..	+	..
Mon.	14	+	..	..	..	+	.	..	..	..
Duf.	13	+	..	..	+	..	..	+	..	..
Sea.	12	+	..	..	+	..	..	+	..	..
Win.	11 (2 sp.)	+	..	..	+	..	..	..	+	..
Par.	10+ (1 sp.)	+	..	..	..	..	+	..	+	..
Ric.		+	.	..	+	..	.	..	..	+
Ne.	8	..	..	+	..	+	..	..	+	..
Doh.	8	..	..	+	..		+	+	..	..
Bur.	6	..	+	..	..	..	+	+	..	..
Nel.	(5) 12	+	..	..	..	+	..	..	+	..
Pa.	Mercury 22, subdural	+	..	..	+	..	..	+	..	..
All.	Mercury, spinal drainage	+	..	..	+	..	..	+	..	..
		16	6	5	12	10	5	9	7	3

The numbers in the columns to the right of the name symbols indicate the number of intravenous injections of arsphenamin, while those in the next column indicate the number of intraventricular and spinal injections.

TABLE 3.—Infiltration in Untreated Patients

	Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Cry.	..	+	..	..	+	..	+	..	..
McN.	..	+	..	..	+	..	..	+	..
McG.	..	+	..	..	+	.	..	+	..
Tin.	..	+	..	..	..	+	..	..	+
Spe.	..	+	..	..	..	+	..	..	..
Tru.	..	..	+	..	+	..	..	+	..
For.	..	..	+	..	+	..	..	..	+
Hub.	..	..	+	..	+	..	..	..	..
Dra.	..	..	+	..	..	+	..	+	..
Bla.	..	..	+	..	.	+	..	+	..
Pim.	..	..	+	..	+	..	..	..	+
Tit.	..	..	+	..	+	..	..	..	+
Fre.	..	..	+	..	+	.	..	..	..
Mas.	..	..	+	..	..	+	..	+	..
San.	..	..	+	..	..	+	..	+	..
	0	5	10	0	9	6	1	7	4

of a common denominator for the two series. The figures here are relative and not actual and represent a graph that would show the proportion had there been the same number in each series.

Table 2 shows the findings in the individual cases arranged in the order of the amount of treatment received. A perusal of this chart will show that the various reactions bear no definite relation to the amount of treatment received, since several of the patients who had received a considerable amount of treatment show more reaction than others who had received a smaller amount. It is also indicated that there is not always a parallelism between the amount of perivascular lymphocytic

TABLE 4.—Infiltration in Treated Patients Arranged According to Age

		Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Age	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Nel.	32	+	..	..	+	..	..	..	+	..
All.	33	+	..	..	+	..	..	+		..
Gal.	33	..	+	..	..	..	+	..	..	..
Per.	34	..	+	..	..	+	..	..	..	..
Uni.	36	+	..	..	+	..	..	..	..	..
Mor.	36	..	.	+	..	+	..	..	..	+
Pai.	38	+	..	..	+	..	..	+	..	..
Bur.	38	..	+	..	..	..	+	+	..	..
Dal.	39	..	+	..	..	+	..	..	..	..
O'B.	39	+	..	..	+	..	..	..	+	..
Hal.	40	..	+	..	+	..	..	+	..	..
Lar.	41	+	..	..	+	..	..	+	..	..
Tho.	41	..	+	..	..	+	..	..	..	..
Ric.	42	+	..	..	+	..	..	..	..	+
Cah.	42	+	..	..	+	..	..	..	..	..
Doh.	42	..	..	+	..		+	+	..	..
Hay.	42	..	..	+	..	..	+	..	+	..
Rey.	43	+	..	..	..	+	..	..	..	..
Smy.	43	..	..	+	..	+	..	..	..	+
Duf.	45	+	..	..	+	..	..	+	..	..
Sea.	46	+	..	..	+	..	..	+	..	..
Par.	49	+	..	..	..	..	+	..	+	..
Ken.	53	+	..	..	+	..	.	..	+	..
Bre.	56	+	..	..	+	..	..	+	..	..
New.	57	..	..	+	..	+	..	..	+	..
Mon.	57	..	..	..	..	+	..	..	..	..
Win.	60+	+	..	..	+	..	..	..	+	..

reaction and the pial reaction in the same case, although in general the relationship is fairly close.

A point of some interest and importance is presented in certain cases in which a considerable amount of treatment has been given (e.g., Table 2, Smy. No. 7). Although this patient had received twenty-two intravenous injections of arsphenamin he showed a considerable amount of pial infiltration. This would seem to indicate that often the pial inflammation is not so readily amenable to antisyphilitic drugs as is ordinarily supposed.

Table 3 shows findings in the untreated cases charted as are the findings of the treated cases in Table 4.

Besides the amount of treatment received, there are other factors which presumably might influence the amount of exudative reaction in this series, such as the age of the patient, the clinical type of the psychosis, its duration and the interval between the last treatment and

TABLE 5.—Infiltration in Untreated Patients Arranged According to Age

		Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Age	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Tru.	34	..	..	+	..	+	..	..	+	..
Tin.	36	..	+	..	..	+	..	..	..	+
Dra.	38	..	..	+	..	..	+	..	+	..
Hub.	43	..	..	+	..	+	..	..	..	..
Spe.	44	..	+	..	..	..	+	..	..	..
McG.	45	..	+	..	..	+	..	..	+	..
Tit.	?	..	..	+	..	+	..	..	..	+
Bla.	49	..	..	+	..	..	+	..	+	..
McN.	52	..	+	..	..	+	..	..	+	..
Fo.	53	..	..	+	..	+	..	..	..	+
San.	54	..	..	+	..	..	+	..	+	..
Pi.	55	..	..	+	..	+	..	..	..	+
Cry.	56	..	+	..	..	+	..	+	..	..
Fre.	60	..	..	+	..	..	+	..	+	..
Mas.	77	..	..	+	..	..	+	..	+	..

TABLE 6.—Type of Psychosis in Treated Patients

	Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Simple Deterioration									
Mor.	..	..	+	..	+	..	..	..	+
Ric.	+	..	..	+	..	..	..	..	+
Sca.	+	..	..	+	..	..	+	..	..
Tho.	..	+	..	..	+	..	..	..	..
Uni. (tabes)	+	..	..	+	..	..	..	..	..
Win.	+	..	..	+	..	..	..	+	..
Doh.	..	..	+	..	..	+	+	..	..
All.	+	..	..	+	..	..	+	..	..
Bre.	+	..	..	+	..	..	+	..	..
Cah. (convulsions)	+	..	..	+	..	..	..	..	..
Dal. (convulsions)	..	+	..	..	+	..	..	..	..
Hal. (tabes)	..	+	..	+	..	..	+	..	..
Mon.	+	..	..	..	+	..	..	..	..
Duf. (convulsions)	+	..	..	+	..	..	+	..	..
Agitated or Depressed									
Hay.	..	..	+	..	..	+	..	+	..
Nel.	+	..	..	..	+	..	..	+	..
O'B.	+	..	..	..	+	..	..	+	..
Smy.	..	..	+	..	+	..	..	..	+
Expansive									
Bur. (tabes)	..	+	..	..	+	..	+	..	..
Par.	+	..	..	..	..	+	..	+	..
Rey.	+	..	..	..	+	..	..	..	..
Confused									
Ken.	+	..	..	+	..	..	..	+	..
Pal.	+	..	..	+	..	..	+	..	..
Per.	..	+	..	..	+	..	..	..	..

the death of the patient. Tables 4 to 9 inclusive indicate the findings arranged in the light of these factors. The only other striking fact brought out by our investigation was that in treated patients dying shortly after receiving treatment there tended to be a greater degree of

TABLE 7.—Type of Psychosis in Untreated Cases

	Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Simple Deterioration									
Pim. (tabes)	..	..	+	..	+	..	..	..	+
Dra.	..	..	+	..	..	+	..	+	..
Fo.	..	..	+	..	+	..	..	..	+
Tin.	..	+	..	..	..	+	..	..	+
McN.	..	+	..	..	+	..	..	+	..
Tru.	..	..	+	..	+	..	..	+	..
Hub.	..	..	+	..	+	..	..	..	..
Agitated or Depressed									
Bla. (tabes)	..	..	+	..	..	+	..	+	..
Fre.	..	..	+	..	..	+	..	..	..
Expansive									
Spe.	..	+	..	..	..	+	..	..	..
San.	..	..	+	..	..	+	..	+	..
Tit.	..	..	+	..	+	..	..	..	+
Confused									
McG.	..	+	..	..	+	..	..	+	..

TABLE 8.—Duration of Psychosis

		Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Duration	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Lar.	5 mos.	+	..	..	+	..	..	+	..	..
Nel.	6 mos.	+	..	..	..	+	..	..	+	..
Gal.	9 mos.	..	+	..	..	..	+	..	..	..
Ric.	2 yrs.	+	..	..	+	..	..	..	..	+
Cah.	2 yrs.	+	..	..	+	..	..	..	..	..
New.	2 yrs. 2 mos.	..	+	..	..	+	..	..	+	..
Rey.	2 yrs. 2 mos.	+	..	..	..	+	..	..	..	..
Mor.	2 yrs. 2 mos.	..	..	+	..	+	..	..	..	+
Per.	2 yrs. 4 mos.	..	+	..	..	+	..	..	..	..
Hal.	2 yrs. 5 mos.	..	+	..	+	..	..	+	..	..
Duf.	2 yrs. 5 mos.	+	..	..	+	..	..	+	..	..
Mon.	2 yrs. 9 mos.	+	..	..	..	+	..	..	..	..
Par.	3 yrs.	+	..	..	..	..	+	..	+	..
Dal.	3 yrs.	..	+	..	..	+	..	..	..	..
Hay.	3½ yrs.	..	+	..	..	..	+	..	+	..
Ken.	3½ yrs.	+	..	..	+	..	..	..	+	..
Pa.	3¾ yrs.	+	..	..	+	..	..	+	..	..
Al.	4 yrs.	+	..	..	+	..	..	+	..	..
O'B.	5 yrs.	+	..	..	..	+	..	..	+	..
Tho.	5 yrs. 5 mos.	..	+	..	..	+	..	..	..	..
Win.	6 yrs.	+	..	..	+	..	..	..	+	..
Sea.	6 yrs.	+	..	..	+	..	..	+	..	..
Doh.	7 yrs. 2 mos.	..	..	+	..	..	+	+	..	..
Uni.	8 yrs.	+	..	..	+	..	..	..	..	..
		No Treatment								
Bla.	3½ mos.	..	..	+	..	+	..	..	..	+
Dra.	1 year	..	+	..	..	..	+	..	+	..
McN.	1 year	..	+	..	..	+	..	..	..	..
Cr.	1 year	..	+	..	..	+	..	+	..	..
San.	1½ years	..	..	+	..	..	+	..	+	..
Hub.	1¾ years	..	..	+	..	..	+	..	+	..
Tru.	3 years	..	..	+	..	+	..	..	+	..
Pi.	3 years	..	..	+	..	+	..	..	..	+
Spe.	4 years	..	+	..	..	..	+	..	..	..

plasmacytic reaction than in patients in whom a lengthy interval had elapsed between the end of treatment and death (Table 9).

We may conclude, therefore, that treatment definitely reduces the amount of plasma cell infiltration in cases of general paresis. This reduction is so striking that the histologic study of the cases gives a fairly good indication of whether the patient had received antisyphilitic treatment or not.

What becomes of the plasma cells if they are not present in treated patients in the same proportion as in untreated patients? If we are to assume with Gruner and Nägeli that plasma cells are the result of

TABLE 9.—Amount of Infiltration in Patients According to Length of Interval Between Last Treatment and Death

		Plasma Cell Infiltration			Lymphocytic Infiltration			Pial Infiltration		
	Interval	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Cah.	8 days	..	+	..	+	..	..	..	..	..
Hay.	14 days	..	..	+	..	..	+	..	+	..
Lar.	14 days	+	..	..	+	..	..	+	..	..
Hal.	1 mo.	..	+	..	+	..	..	+	..	..
Gal.	1 mo.	..	+	..	..	..	+	..	..	..
Dal.	1 1/10 mos.	..	+	..	..	+	.	..	..	..
Per.	1 1/2 mos.	.	+	.	..	+	..	..	..	..
Nel.	1 1/4 mos.	+	..	..	..	+	..	..	+	..
Ric.	2 1/6 mos.	+	..	..	+	..	..	..	..	+
Bu.	2 1/2 mos.	..	+	..	..	..	+	+	..	..
O'B.	2 1/2 mos.	+	..	..	..	+	.	..	+	..
Mon.	3 1/4 mos.	+	..	..	..	+	.	.	..	..
Pa.	4 mos.	+	..	..	+	..	..	+	..	..
Uni.	4 mos.	+	..	..	+	..	..	..	..	..
Smy.	4 1/6 mos.	..	..	+	..	+	..	..	..	+
Doh.	6 mos.	..	..	+	..	..	+	+	..	..
Rey.	8 mos.	+	..	..	..	+	..	..	..	..
Par.	1 year	+	..	..	..	..	+	..	+	..
Duf.	1 year	+	..	..	+	..	..	+	..	..
Win.	1 yr. 1/2 mo.	+	..	..	+	..	..	..	+	..
Mor.	1 yr. 1 mo.	..	..	+	..	+	..	..	..	+
Bre.	1 yr. 3 1/2 mos.	+	..	..	+	..	..	+	..	..
Ken.	1 yr. 6 mos.	+	..	..	+	..	..	..	+	..
Sca.	1 yr. 6 mos.	+	..	..	+	..	..	+	..	..
Tho.	1 yr. 10 mos.	..	+	..	..	+	..	..	..	..
New.	1 yr. 11 mos.	..	..	+	..	+	..	..	+	..
All.	3 yrs. 3 mos.	+	..	..	+	..	..	+	..	..

irritation, it might follow that the amount of irritation produced by the spirochete had been reduced as a result of treatment and thus less tendency existed for the formation of plasma cells. Or it is possible that arsphenamin may provoke a more acute reaction than occurs in patients with untreated paresis. This would be similar to the so-called arsphenamin neurorecidives. In either case the conclusion would be that treatment had produced the change through its antispirochetocidal properties. It does not seem probable, however, that the reaction produced is of the type of the neurorecidive as it occurs in patients that have received a great deal of treatment, whereas the arsphenamin

neurorecidives occur after the first few treatments; further, there is a decrease in the lymphocytes while in the neurorecidive there should be an increase in these elements. Therefore it seems most likely that the decrease in plasma cells and lymphocytes represents a lessening of the irritative phenomena.

No definite differences are noted, so far as the glia reaction is concerned, between treated and untreated patients. This relates both to the ameboid glia, the round glia cells, and also to the rod cells. Tables 10 and 11 indicate the findings in the two series.

Several points of general clinical interest have come to our attention in this study. It would seem that the cell count of the cerebrospinal

TABLE 10.—Glia Reaction in Treated Patients

	Round Glia			Rod Cells			Ameboid Glia		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Dal.	..	+	..	..	..	..	..	..	+
Uni.	..	+	..	..	..	..	..	..	+
Cah.	..	..	+	..	..	..	..	..	+
Hal.	..	+	..	..	..	..	..	..	+
O'B.	..	....	+	..	+	..	..	+	..
Smy.	..	+	..	+	..	..	..	+	..
Lar.	..	+	..	..	..	..	..	..	+
Per.	..	+	..	..	..	..	..	..	..
Hay.	..	..	+	..	+	..	..	+	..
Gal.	..	+	..	..	..	..	..	+	..
Mor.	..	+	..	..	..	..	..	..	+
Bre.	..	..	+	..	..	+	..	..	+
Tho.	..	+	..	..	+	..	..	+	..
Ken.	..	..	+	..	..	+	..	..	+
Mon.	..	+	..	..	..	..	..	+	..
Duf.	..	+	.	..	+	..	..	+	..
Sea.	..	..	+	..	..	..	..	+	..
Win.	+	..	..	..	..	..	..	..	..
Par.	..	+	..	..	..	+	..	..	+
Ric.	..	+	..	..	..	..	..	+	..
New.	..	..	+	..	..	..	..	..	+
Doh.	..	..	+	..	..	..	..	..	+
Bur.	..	..	+	..	..	+	..	..	+
Pai.	+	..	..	..	+	..	..	..	+
Nel.	+	..	..	..	..	..	..	..	..
All.	..	..	+	..	..	+	..	..	..
	3	13	10	1	5	5	0	10	13

fluid obtained from the lumbar region during life does not give a satisfactory indication of the extent of the cerebral meningitis; that is, it gives little evidence of cellular infiltration of the meninges. Thus in two of the patients from the untreated group (Fo. and Pi.) who had a marked pial infiltration, the cell count of the spinal fluid was 10 per cubic millimeter in one and 14 per cubic millimeter in the other, whereas two others of this group (McG. and Da.) who had a moderate meningeal involvement, that is less than Fo. and Pi., showed 17 and 93 cells per cubic millimeter, respectively.

Similar observations were made in patients treated. For instance, Mo., who had marked meningitis, had a cell count in the spinal fluid varying from 2 to 4 cells per cubic millimeter on several occasions. Similarly Par., who had a marked lymphocytic infiltration of the pia, had a cell count that was within normal limits on all but two occasions, the following numbers indicating the cell count per cubic millimeter on successive examinations: 2, 0, 17, 2, 2, 6, 2, 3, 5, 1, 0, 0, 8, 2, 3, 4, 2, 0, 6 (Fig. 10).

In contrast, Ha., who had no greater amount of pial involvement, had cell counts of 20, 35 and 55 cells per cubic millimeter on three successive examinations; Doh. and Bu., who had slight infiltration of the cerebral meninges, had cell counts of 18 and 20, respectively.

Our material further proves that the colloidal gold reaction may become negative as a result of treatment in cases of general paresis.

TABLE 11.—Glia Reaction in Untreated Patients

	Round Glia			Rod Cells			Ameboid Glia		
	Slight	Moderate	Considerable	Slight	Moderate	Considerable	Slight	Moderate	Considerable
Tru.	..	+	..	..	..	+	..	+	..
Pim.	..	+	..	..	..	..	..	+	..
McN.	..	+	..	..	+	..	..	+	..
McG.	..	+	..	..	+	..	..	+	..
Mas.	..	+	..	..	+	..	+	..	..
Tit.	..	+	..	..	..	..	..	+	..
San.	..	+	..	..	..	..	..	..	+
Cry.	..	..	+	..	..	+	..	..	..
Fo.	..	..	+	..	..	..	..	..	+
Hub.	..	..	+	..	+	..	..	..	+
Dra.	..	..	+	..	..	+	..	..	+
Bla.	..	..	+	..	..	..	..	..	..
Fre.	..	..	+	..	..	+	..	..	+
Tin.	..	..	+	..	..	+	..	..	+
Spe.	..	..	+	..	..	..	..	..	+
	0	7	8	0	4	5	1	5	7

This is an observation which has, of course, been made clinically a number of times: that is, in cases clinically labeled general paresis a so-called paretic curve present at the outset of treatment has become normal during treatment. Our point is that we have been able to confirm the diagnosis of paresis by postmortem examination in such cases. For instance, in the case of Dal., numerous colloidal gold tests were made which either were negative or gave a mild reaction; necropsy showed definitely the histologic changes of general paresis. Similar variations from a paretic gold curve to a normal curve occurred in other patients of this group during the course of treatment, and in these cases the diagnosis was confirmed by histologic examination.

What has been said of the colloidal gold reaction is equally true of the Wassermann reaction. The Wassermann reaction in cases of general paresis may become negative as a result of treatment. This in

no way disproves the diagnosis of paresis, and the disease may progress and the patient may die. This occurred in several cases, for example, in the cases of O'B. and Mon. In the latter case (Mon.), the Wassermann reaction became negative in dilutions from 0.1 to 1 c. c. of spinal fluid; the cell count fell to within normal limits, and the gold reaction was much reduced. Nevertheless, the patient died with the signs and symptoms of general paresis, and necropsy confirmed the diagnosis both grossly and histologically.

As is well known, the ventricular fluid in cases of general paresis is entirely negative in some cases and positive in others. In our series

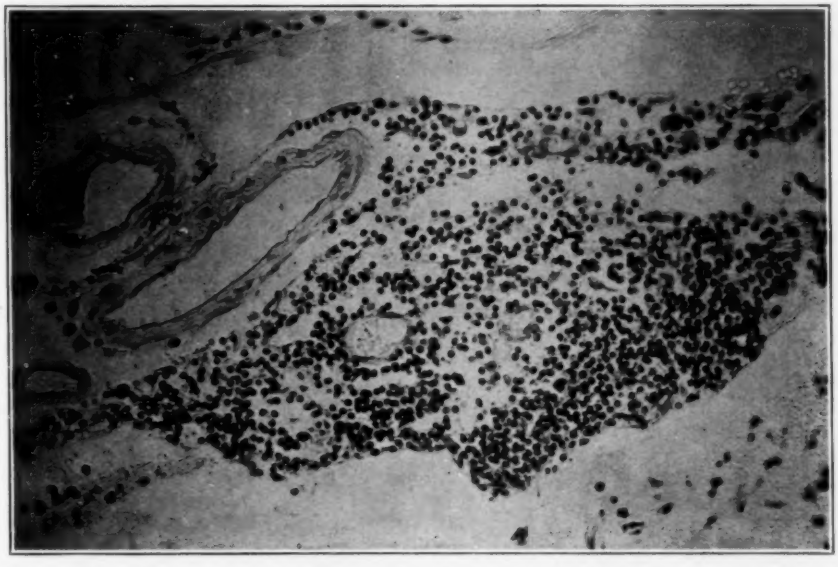

Fig. 10.—Meningitis in patient with paresis who had been treated. Treatment did not remove the infiltrate that is supposed to react readily to antisyphilitic drugs. However, the cell count in the spinal fluid was low, giving no indication of the amount of cerebral meningitis.

there were three patients who had been receiving ventricular injections. In one (Gal.), the ventricular fluid was quite normal, whereas in the other two (Un. and Hal.) the ventricular fluid showed findings in keeping with the spinal fluid in cases of general paresis; namely, positive reactions in the Wassermann, colloidal gold, globulin, and albumin tests. In all three cases the postmortem examination confirmed the diagnosis of general paresis, and no significant differences were observed in the histology of these cases. The negative findings in the ventricular fluid probably indicate a relative imperviousness of the foramina of Lushka and Magendie so that the elements producing

these reactions do not have easy access from the subarachnoid space to the ventricles or that the flow of fluid from the ventricles to the subarachnoid space is active and in that direction almost exclusively.

The inference to be drawn from those cases in which the patient had received intraventricular injections of arsphenamized serum is that no damage is done by such injections. Clinically, there is no evidence of damage nor does the examination of the ventricular fluid subsequent to the injection show any evidence of irritation or inflammation. Thus, in the case of Gal., the ventricular fluid remained negative after the intraventricular injections, and in the other two cases there was no cellular reaction resultant on such treatment. Histologically the ventricular surfaces and the choroid plexus showed no evidence of trauma. We may, therefore, conclude that the introduction of arsphenamized serum into the ventricles does not produce any reactions which contraindicate this type of treatment. On the other hand, we have no evidence from the limited material in which ventricular injections were made that any strikingly good results were accomplished. It seems fair to emphasize that the three patients of this series who received ventricular injections showed no clinical improvement, whereas other patients receiving similar treatment have shown marked improvement. It is at least possible, if not probable, that the findings in the patients who improved with this treatment (not included in this series) would have shown more histologic evidence of this treatment. This statement is in consonance with one made at the beginning of the article calling attention to the fact that all the material available in this study is from patients who did poorly from a clinical standpoint.

SUMMARY

In order to determine whether antisyphilitic treatment produces any effect on the paretic process in the cerebrum that can be recognized histologically, a study was made of brains from cases of general paresis. The series studied was made up of two groups: twenty-seven brains from patients who had received antisyphilitic treatment during the period of the psychosis and fifteen brains from patients who had not received antisyphilitic treatment subsequent to the onset of symptoms of paresis. It was not possible to draw any conclusions concerning parenchymatous changes, nor concerning the true vascular or neurologia changes from a comparison of the two groups. That no significant comparative changes would be shown was to be expected because of the nature of the pathology of these structures in general paresis.

However, the inflammatory reactions, perivascular and pial infiltration, offer theoretically a satisfactory basis for comparison. The degree of cellular infiltration in one case can be compared with the degree of

infiltration in another case. Further, this type of reaction is apparently the result of irritation by a toxic agent. If the activity of the agent is reduced, one expects a reduction of the inflammatory process. This is what happens in cases of tertiary cerebrospinal syphilis in which the patients receive treatment. Plasma cells diffusely present in the perivascular and pial infiltration is the critical finding in general paresis. Hence, a comparative study was made of the amount of perivascular plasmacytic and lymphocytic infiltration and pial reaction in the treated and untreated groups. It was found that plasma cells were few and infrequent in most of the treated patients, especially in comparison with the untreated ones. This was so striking that in many cases it was possible to predict from the histologic picture whether or not the patient had received treatment. The lymphocytic perivascular infiltration was also much less, on the whole, in treated than in untreated patients. This was not as striking, however, as the apparent reduction of plasma cells. We believe that the plasma cells are an indication of a chronic irritation, and it seems probable that the reduction of this element in the treated patient is similar to that which occurs in the treatment of an indolent ulcer in which in the course of improvement the more chronic type of reaction is replaced by a more acute and active reaction. If this is true, it would seem to indicate that treatment had influenced the paretic process to a certain degree in most of the cases of our series.

The pial infiltration was likewise strikingly less in the treated than in the untreated patients as a group. However, in some patients who had received treatment the pial infiltration was of considerable extent, indicating that at times systemic antisyphilitic treatment (at least in moderate amounts) is incapable of greatly influencing cerebral meningitis. This is in keeping with clinical observations in cases of simple cerebral meningitis.

The charts show the results of the studies concerning these points.

Neither the age of the patient, the clinical variety of the psychosis, nor its duration seemed to have any distinct bearing on the amount of cellular inflammatory reaction.

CONCLUSIONS

1. Antisyphilitic treatment of patients with general paresis affects the histologic picture.

2. It tends to reduce the plasma cell infiltration of the perivascular spaces, so that in many cases there are fewer plasma cells than are commonly found in untreated cases.

3. This reduction of the plasma cell reaction is probably an evidence of lessened chronicity of the process.

4. Perivascular lymphocytosis is often reduced in amount by treatment.

5. Pial inflammation is often reduced in amount by treatment.

6. Intraventricular injections of arsphenamized serum ordinarily produce no injurious effects on the choroid plexus or ependymal lining of the ventricles.

7. The cell count of the spinal fluid does not give a true indication of the amount or extent of cerebral meningitis.

8. The colloidal reaction, Wassermann reaction and cell count of the spinal fluid in paresis may become negative during treatment.

DISCUSSION

DR. BERNARD SACHS, New York: I should like to know whether there is any reason to suppose that this plasmacytic reaction has any effect on the underlying morbid process, such as general paresis.

DR. HENRY VIETS, Boston: I believe that Dr. Solomon's view is important from the clinical standpoint. If spinal fluids become negative, we cannot depend very much on the reaction of the cerebrospinal fluid in the treatment of our patients.

DR. HERMAN H. HOPPE, Cincinnati: Recently I have been treating paretic patients with the hypertonic salt solution, followed six hours later by an intravenous injection of arsphenamin. Several of these patients became violent, this state lasting from twenty-four to thirty-six hours. In all of the cases we obtained some acute cortical reaction.

DR. BERNARD SACHS, New York: Is this perhaps the result that one might have expected after the nucleate of soda injections that were in favor with many physicians a number of years ago? It is interesting to note the effects of the use of various remedies which were so popular in the past.

DR. PETER BASSOE, Chicago: I wish to relate the case of a physician with rather advanced paresis, who received quite intensive Swift-Ellis treatment. After the last injection he contracted a severe streptococcic sore throat which was followed by a streptococcic meningitis, of which he died. An examination of the brain revealed a marked decrease in the amount of perivascular infiltration. In fact, a great number of the perivascular spaces in the cortex showed practically no cells; they showed loose connective tissue network almost free from either lymphocytes or plasmacytes. I suppose we cannot assume that an acute meningitis which lasted a few weeks would bring about a change of that kind, so that perhaps the condition may be ascribed to the previous treatment.

DR. SOLOMON, in closing: In regard to Dr. Sachs' question as to the important underlying morbid process in general paresis and the relation to the plasmacytic reactions so commonly found, I can give no satisfactory reply. I do not know why plasma cells occur, unless it is a response to a toxic agent acting over a long period. We look on the plasma cell as one evidencing a chronic type of reaction. Recent work by Jahnel, Jakob, and Valente apparently shows that spirochetes are present in large numbers, particularly where activity is most marked. We have not had a technic that was sufficiently good to attempt to show spirochetes. It would be interesting to know whether in these cases the spirochetosis had been decreased or increased.

There were several of these patients that had the miliary gummas in various spaces scattered throughout, and those patients invariably had the lymphocytic and plasmacytic reaction about the gummas irrespective of whether it was to be found elsewhere.

One of the patients in this series had received sodium nucleinate injections, also ventricular, spinal and a considerable number of intravenous injections. He showed a large amount of lymphocytic reaction. Unfortunately, however, I did not have the pia to examine, but it seemed to have more reactive cells than in most of the cases. Otherwise I have no knowledge of the exact effect of sodium nucleinate.

Dr. Kolmer and Dr. Lucke's article concerning the findings in the monkeys and rabbits treated with mercury has always been a mystery to me, unless the condition is similar to a lead encephalopathy.

Hypertonic salt solutions followed by intraspinal injections cause a tremendous reaction of the patient, fever, vomiting, nausea and headache, but we have not experienced so much reaction with the intravenous injections. About 100 c.c. of 15 per cent. salt solution does not give much change in the cerebrospinal fluid pressure, which we observe for approximately five hours.

In regard to the colloidal gold and Wassermann reactions, we have found in only two cases that the gold became negative, which shows that it could happen in cases of paresis confirmed by necropsy. In these cases the globulin reaction was positive. The gold reaction, as is known, is the result of the balance between the albumin and globulin. The colloidal gold reaction may be negative although globulin remains present, as in my cases. By a negative gold reaction is meant a reaction of one plus or less.

We had a patient similar to Dr. Bassoe's, a juvenile paretic who developed an acute cerebrospinal meningitis as the result of a faulty technic in intraspinal injection. She died four weeks later of cerebrospinal meningitis, and at necropsy the meninges showed a peculiar gummy type of reaction, almost free from cells, which was difficult to understand.

PROGRESSIVE FUNICULAR MYELOPATHY (SUBACUTE COMBINED DEGENERATION)*

JOSEPH H. GLOBUS, M.D., AND ISRAEL STRAUSS, A.M., M.D.
NEW YORK

Most investigators agree that the clinical entity known as subacute combined degeneration or subacute funicular myelitis is not a true system disease, but that the disease process begins in numerous more or less irregularly distributed foci, which later coalesce.

Shimozono [1] and Wohlwill,[2] employing modern methods, attempted to establish the sequence of the disease process. Their aim was to discover the structural unit which first suffers. They claim that the axis cylinder is first attacked and that the other changes are secondary.

Shimozono studied three cases of pernicious anemia and a number of experimental animals in which severe anemia was produced by the injection of pyrodin. He concluded that the disease process was mainly neurolytic. He describes the axis cylinder changes as occurring in three distinct phases. First, there is slight swelling in the axis cylinder leading to irregularities in its outline; second, there is loss of staining properties and loss of fibrillar structure, and finally, dissolution. He attributes great importance to the presence in large numbers of so-called Elzholz bodies. In his description of these bodies he does not differ from that of Elzholz.[3] They are small round bodies, staining like Marchi bodies. They occur most commonly in the neighborhood of the node of Ranvier and for some distance between the myelin sheath and the membrane of Schwann. They are also frequently seen in the nuclei of the neurilemma cells, where they have an eccentric position and tend to herniate into the surrounding cytoplasm. They are considered by Shimozono as indicative of primary degeneration in the axis cylinder. Elzholz considered them products of decomposition. Their staining reactions suggest their origin from myelin. Elzholz also found these bodies in normal nerve fibers, though not in as great numbers as in diseased nerves. This led him to suggest that they may be the product of metabolic changes in the myelin. Shimozono's inter-

---

* From the Neurological Service and the Pathological Laboratory of the Mount Sinai Hospital.

* Read at the Forty-Eighth Annual Meeting of the American Neurological Association, Washington, D. C., May, 1922.

1. Shimozono: Deutsch. Ztschr. f. Nervenheilk. **35**: 1908; Arch. f. Psychiat. **53**:972, 1914.

2. Wohlwill: Deutsch. Ztschr. f. Nervenheilk. **68-69**:423, 1921.

3. Elzholz: Jahrb. f. Psychiat. u. Neurol. **17**: 1897.

pretation of the axis cylinder involvement as primary is still doubtful. One would not expect to find well preserved axis cylinders in an area of destruction of long standing were the axis cylinder the first structure to be attacked. We shall show that naked axis cylinders are frequently encountered in the diseased foci. Again, the occurrence of hemorrhages in the material which he studied led Shimozono to the hypothesis that the blood which has escaped from a partially injured blood vessel undergoes decomposition and liberates certain products which are specifically detrimental to the axis cylinders. These hemorrhages are infrequent, according to the reports of other investigators, as well as in the material used in the present study, and may be altogether absent. Hence we are not warranted in assigning to them a specific causative action. Schroeder [4] observed hemorrhagic extravasations in the so-called "Ringwall-Herdchen." He takes the ground, however, that these mild hemorrhages cannot be considered as causative factors in the disease process of pernicious anemia. The absence of adventitial changes in the involved blood vessels, in his opinion, points to the probability that these extravasations play a secondary rôle.

Wohlwill, in a large number of cases, found anatomic features similar to those described by Shimozono. He also considers the so-called neurolytic swelling the first step in the disease process. He based his observations, however, on the finding of one single nerve fiber, which he studied in cross section. He claims that one almost never sees intact axis cylinders in the path of the degenerated myelin sheaths, and that the process in this disease differs thus from that in multiple sclerosis. The demyelinization here is secondary to the axis cylinder dissolution. On the other hand, he describes ball-like terminations in some axis cylinders, similar to those found by Marinesco and Minea in multiple sclerosis.

Hassin's [5] observations in two cases of subacute combined cord degeneration led him to conclude that the "lesion affects principally the myelin, the axones becoming affected later on, when we have before us the picture of Wallerian degeneration....." "The process of destruction," he continues, "begins in the myelin, later involves the axone, finally resulting in Wallerian degeneration."

REPORT CF CASES

CASE 1.—*History.*—H. N., a woman, aged 57 years, was admitted to the hospital on April 11 and died on April 23, 1921. Two brothers had died of pulmonary tuberculosis. The patient, until the onset of the illness, had been well. The present illness began gradually, six months previous to admission, with a feeling of weakness in the lower extremities, which was at first more

4. Schroeder: Monatschr. f. Psychiat. u. Neurol. **35**: 1914.
5. Hassin: Med. Rec. 1917.

marked in the left leg. Within four weeks she was completely paralyzed in both legs. At the same time the extremities felt numb and she occasionally suffered from paresthesia. A gradual wasting was noticed in both lower limbs. Six weeks before admission she lost control of the bladder and rectum, and superficial ulcers developed over the buttocks. The strength in the muscles of the trunk and upper extremities was well preserved.

Physical Examination.—The patient was a fairly well developed woman with marked pallor of the skin. There was bilateral ptosis, more marked on the right. The pupils reacted equally to light and accommodation. Horizontal nystagmus on lateral fixation was present. The fundi were normal. There was general atrophy of both upper extremities, with marked wasting in the interossei. Moderate hypotonia; marked incoordination, and adiadokokinesis; marked wasting, hypotonia and almost complete paralysis of both lower extremities were present. Deep reflexes were present in the upper extremities, and absent in the lower. The abdominal reflexes were lost. A bilateral Babinski sign was present. There was general hypalgesia. Temperature, muscular and vibratory senses were lost.

Blood Examination.—The blood was examined twice. The first examination revealed: 3,500,000 red cells; 65 per cent. hemoglobin; 8,000 white cells; 74 per cent. polymorphonuclears; anisocytosis; some cells hyperchromatic, and a few macrocytes. The hemoglobin index was 1.1. The second examination revealed: 2,820,000 red cells; 65 per cent. hemoglobin; platelets, 304,000; white cells, 3,800; 39 per cent. polymorphonuclears; 58 per cent. lymphocytes; 2 per cent. eosinophils; 1 per cent. monocytes; coagulation time, seven minutes; bleeding time, one and a half minutes. A note by Dr. Rosenthal reads as follows: "Hyperchromatic anemia showing numerous macrocytes, polychromatophilia and some anisocytosis, apparently resembling pernicious anemia. Blood platelet count, however, is unusually high."

Course of Illness.—On the day before the patient's death, speech became nasal, breathing labored and swallowing difficult. There was some exophthalmos, facial paresis, more marked on the left side, and increased weakness in the upper extremities. Atrophy of the intrinsic muscles of the hand increased. The reflexes of the upper extremities were increased. Memory was poor. The patient was easily fatigued. The pulse was very rapid.

CASE 2.—*History.*—M. B., a woman, aged 68 years, was admitted to the hospital on Aug. 26, 1921, and died on Sept. 9, 1921. She gave no history of previous illness. Seven months before admission she complained of a peculiar tingling in the fingers of both hands. This paresthesia became persistent; at the same time general weakness developed, accompanied by loss of weight.

Physical Examination.—The patient was a poorly nourished woman, very anemic and extremely weak. There were no changes in the innervation of the cranial nerves. The reflexes were normal; no paralyses and no gross changes in sensation were present.

Blood Examination.—Examination revealed 2,000,000 red cells; hemoglobin, 55 per cent.; color index, 1.3; white cells, 4,800; polymorphonuclears, 58 per cent.; lymphocytes, 40 per cent.; monocytes, 2 per cent.; red cells showed hyperchromia, polychromatophilia, poikilocytosis and anisocytosis. Two later examinations showed gradual increase in the color index to 1.4. Gastric analysis disclosed absent free hydrochloric acid. The total acidity was 33.

Course of Illness.—During her stay in the hospital, the patient developed mental disturbance. She became disoriented, speech was incoherent at times, and there was a mild muttering delirium. Definite lateral nystagmus appeared in both eyes, and ataxia of the left arm developed. The knee reflexes were lost.

Pathologic Anatomy.—Material and Methods: The spinal cords of the patients in Cases 1 and 2, and the brain in Case 1, were available for study. Numerous blocks were fixed in liquor formaldehydi, alcohol and Weigert's glia mordant. Some formaldehyd fixed material was further carried into Müller's fluid and into Müller-osmic-acid solution. Celloidin, paraffin and frozen sections were made. The following stains were used: Delafield's hematoxylin, Heidenhain's iron hematoxylin, Spielmeyer's myelin sheath stain, Weigert-Pal, Marchi, Herxheimer's fat stain, Bielschowsky's silver, Alzheimer-Mann and Jacob's methods.

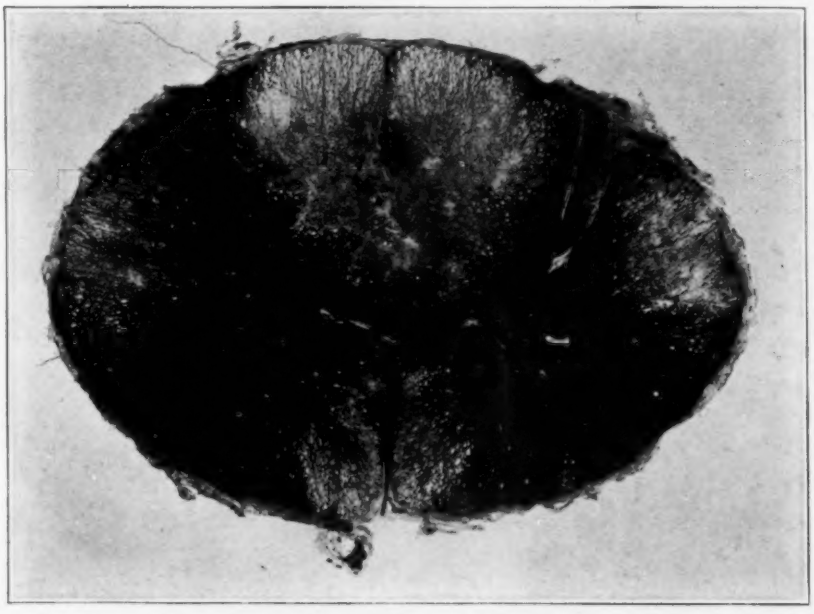

Fig. 1 (Case 1).—Section of a dorsal segment showing the almost complete involvement of the dorsal, lateral and anterior pyramidal tracts.

Gross Anatomy: Both spinal cords appeared markedly reduced in size. The meninges presented no evidence of gross pathologic change. Several cross cuts made in the cord showed a distinct degenerative process in the dorsal, lateral and ventral columns. In Case 1 the lateral and anterior pyramidal tracts showed a most intense destructive process in the lumbar region. In the cervical segments a destructive process in the region of the spinocerebellar tracts was added. The areas involved were best brought out in stained preparations, presenting a picture of distinct combined funicular disease (Fig. 1). A section in the dorsal region, stained by the Marchi method, showed by the appearance of large areas staining black that the process was still active.

Microscopic Anatomy.—In studying the diseased areas in the spinal cord, two grades of process were found. There were lesions which showed active

destructive or regressive process and other areas, irregular in distribution, giving evidence of a more or less chronic, productive reaction. In the acute lesions the extent of the process of dissolution was impressive, large zones of white matter being replaced by products of softening and by phagocytes. This resulted in a cribriform appearance. In preparations stained with scarlet red, such an area of softening showed numerous granular cells (gitter Zellen), and vessels whose adventitial spaces were filled with granular cells loaded with fat. In the chronic foci there was progressive healing by formation of glia fibers.

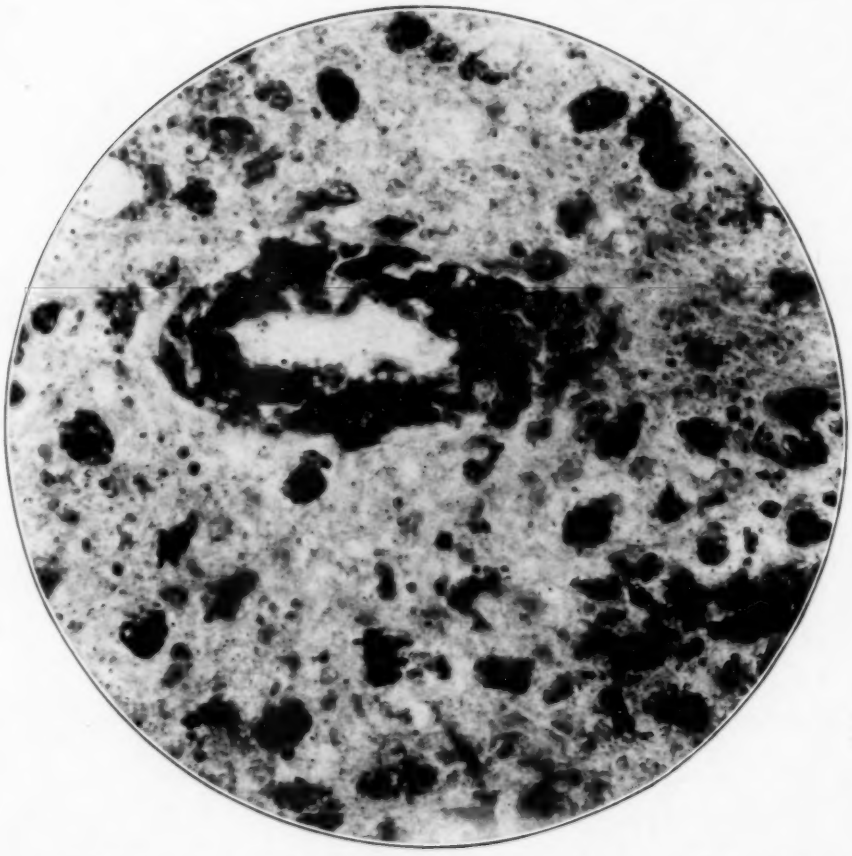

Fig. 2.—Section of an area in the dorsal region of the spinal cord, showing an intense degenerative process evidenced by the presence of large numbers of granular cells loaded with fatty particles. A small vessel surrounded and infiltrated by gitter cells is seen in the field. Vessels of this character are found in large numbers throughout the diseased area of the cord.

In the acute destructive lesion it was highly important to attempt to establish the sequence of events with reference to the involvement of the various structural units including the myelin sheath of nerve fibers, the axis cylinders, the interstitial supporting glial elements, the ganglion cells of the gray matter, and also the mesodermal structures, particularly the blood vessels.

The Myelin Sheath: Our material showed conclusively and uniformly that the myelin sheath was the seat of the most intense disease process. In areas in which the softening process was most acute, the myelin cover of nerve fibers almost completely disappeared. The resultant products of destruction were picked up by phagocytic elements (Fig. 3) which were mainly glial in origin. Where the myelin still remained it was fragmented and occasionally incorporated in Marchi bodies. Transitional stages in the degenerative process of the myelin were frequently seen in the form of swelling or irregularities in outline.

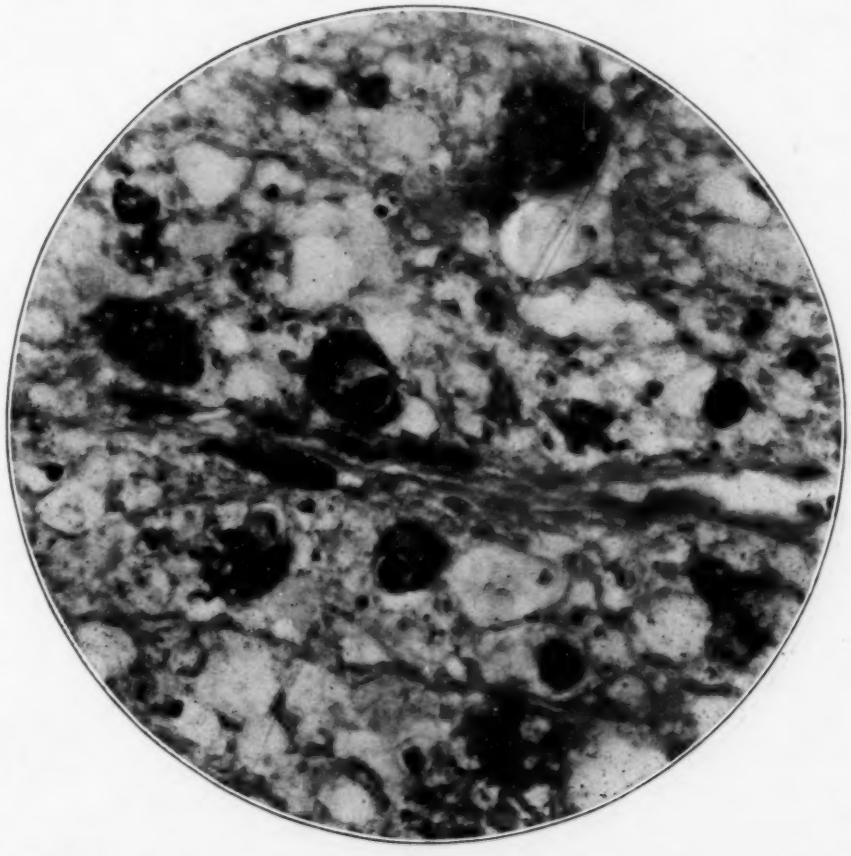

Fig. 3.—Gitter cells of various types containing lipoid particles are shown in relation to blood vessels. Some of the gitter cells contain definite enclosures (myelophages).

Axis Cylinders: The axis cylinders showed changes which, in our opinion, were proportional to the structural modifications noted in the myelin sheaths. The axis cylinders had been involved in the process secondarily to, or in some instances coincidentally with, the destruction of the myelin sheath. This view is based on the fact that in many scars devoid of myelin coat and normal nerve fibers there were naked axis cylinders, fairly uniform in outline, uninterrupted in their course and showing practically no pathologic changes

(Fig. 4). We are not in accord with the observations of Shimozono or Wohlwill, but support the studies of Hassin. It is true that there exist numerous naked axis cylinders which show advanced pathologic changes, such as vacuolization, fragmentation, swelling, cork-screw formation and ball-like terminations. These changes, however, in our opinion, are secondary. With the swelling of the myelin sheath there commonly occurs a coincident change in the outline of the axis cylinder, and as the pathologic process in the myelin sheath advances, the change in the axis cylinder progresses. Complete destruction of the myelin sheath leads eventually to dissolution of the axis cylinders.

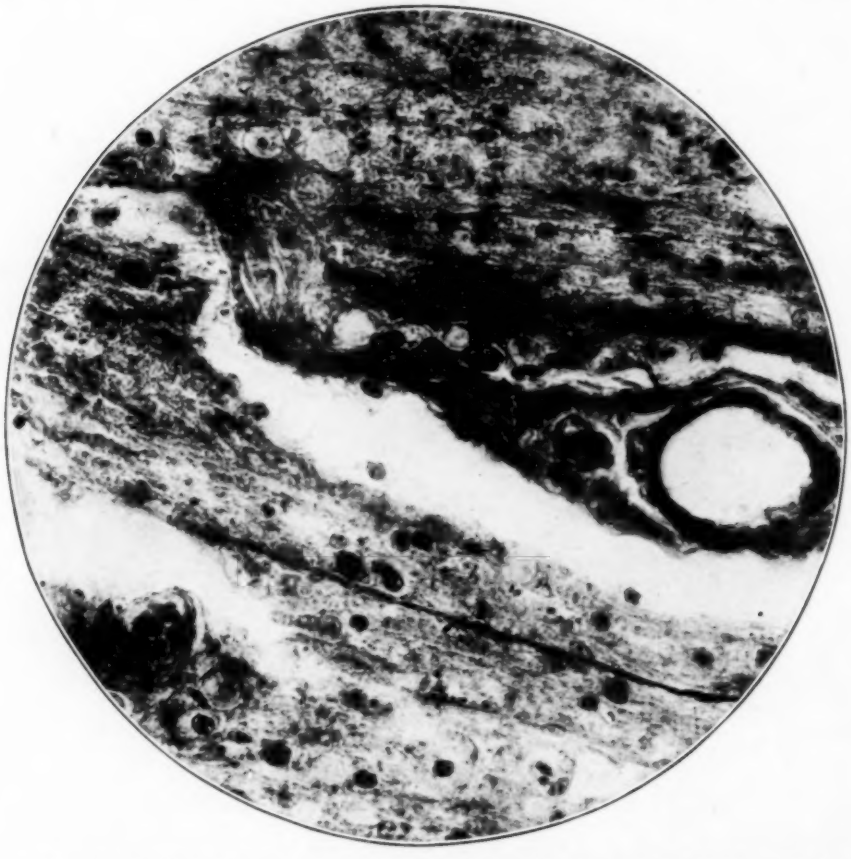

Fig. 4.—Section through an area of softening showing a naked axis cylinder fairly uniform in outline, free of myelin sheath, and surrounded by numerous granular cells; occasional Elzholz bodies.

Elzholz Bodies: These were everywhere in large numbers, particularly in areas of acute softening. They occurred along the course of naked axis cylinders between myelin sheaths and neurilemma, and independent of axis cylinders or myelin sheaths. The lack of uniformity in distribution, the absence of a definite relationship to axis cylinder or to myelin sheath, leads us to conclude that they cannot be looked on as an indication of primary axis cylinder disease.

Glia: The most striking histologic changes were offered by the reactions of the various types of glia elements in both acute and chronic areas of degeneration.

Granular cells were found in extremely large numbers wherever the destructive process was still in progress. They occurred in close proximity to naked axis cylinders, within nerve fibers, where they had replaced the myelin, in the interstices formed by the reticular network of the normal neuroglia and occasionally with no trace of myelin or axis cylinder in the vicinity. Again, they were found in large numbers in the adventitial coat of blood vessels, occasion-

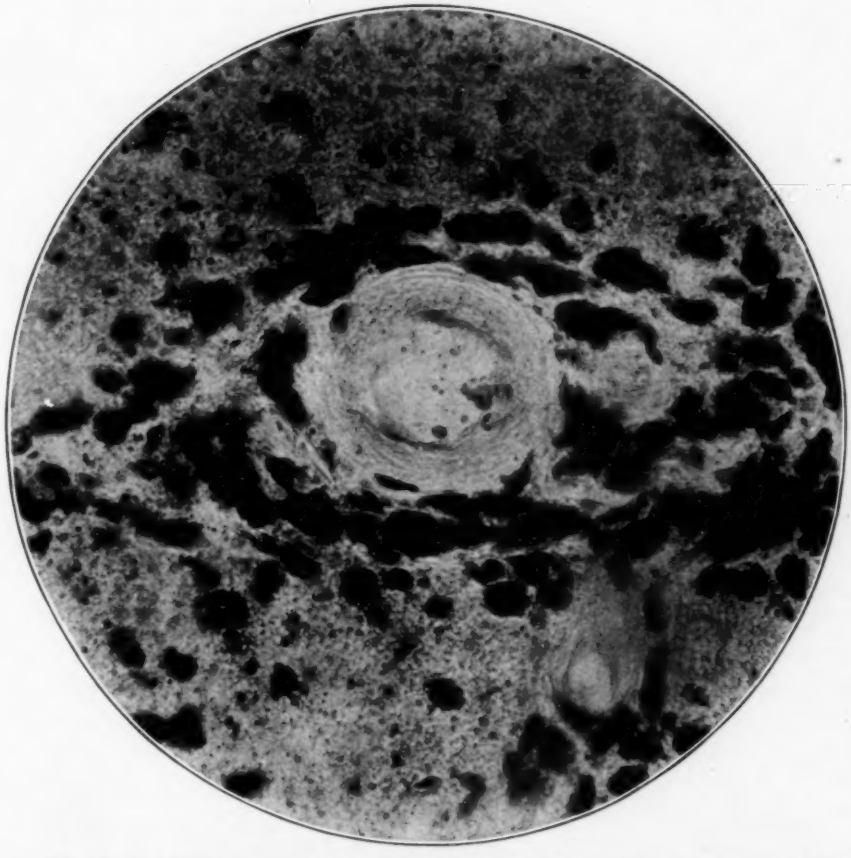

Fig. 5.—A blood vessel in an area of acute degeneration, showing marked adventitial infiltration with the media and intima intact and unmodified.

ally forming several layers about a small vessel (Fig. 5). When stained by fat stains they were seen to be crowded with large fat droplets. On the other hand, when the fat content was washed out by the clearing agent in the process of embedding, their cytoplasm had a reticulate appearance.

The fiber-forming, or monster, glia cells were found (Fig. 6) in areas in which the regressive process was complete and the organizing process was in progress. They were most common in the vicinity of blood vessels and sent processes to the adventitial coat of the blood vessel. Naked axis cylinders were frequently found in these areas of gliosis.

Blood Vessels: The adventitial spaces (Virchow-Robin) of the small and medium-sized vessels, as well as of an occasional larger vessel, were crowded with fat-containing granular cells. The adventitial connective tissue of some of the vessels underwent a marked proliferation. In some instances there was an apparent thickening of the adventitial coat. These changes, however, cannot be interpreted as an inflammatory reaction. There were no well defined pathologic changes in the adventitia, media or intima of the blood vessels throughout the spinal cord, which would suggest an inflammatory or even a

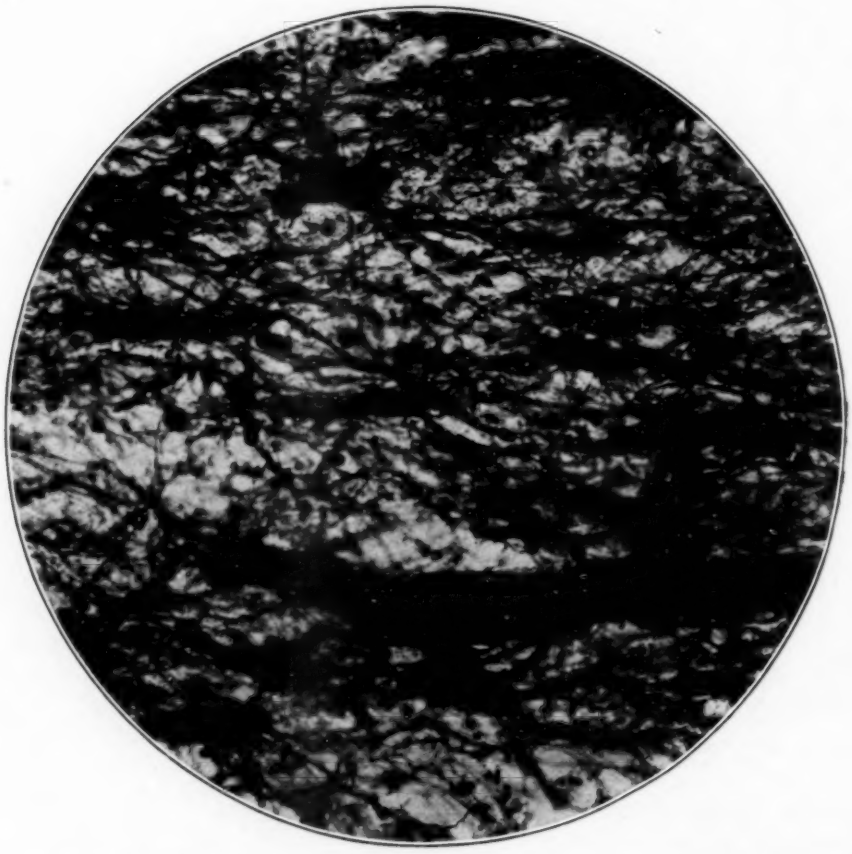

Fig. 6.—Gliosis in the area of the scar showing many monster glia forming cells, arranged about a medium sized blood vessel.

degenerative change in the wall of the blood vessel. While occasionally there appeared to be some tendency toward the hyalinization of the media or a slight increase in the size of an endothelial cell of the intima, there was no definite evidence of an endarteritis or other disease of the blood vessels.

Brain: A systematic study of numerous sections from the brain stem and cerebral hemispheres in Case 1 showed only small areas of perivascular softening, with an accumulation in the vicinity of the vessel of a limited number of "gitter" cells and occasional amyloid bodies. The vessels themselves showed

only moderate change. In some there appeared a deposit of a slight amount of yellowish pigment in the intima, with no change in the lining cells, while in others the adventitia showed an accumulation of fairly large quantities of lipoid material, without change in the media and intima.

Spinal Roots: Preparations showed deposits of fat and Marchi bodies.

SUMMARY

It is quite evident that the morbid changes found in so-called combined system disease are to be regarded as degenerative in character. The almost total absence of a reaction on the part of the mesodermal components excludes an inflammatory origin. For this reason the term "subacute funicular myelitis," first suggested by Henneberg, is inaccurate. With Spielmeyer and Wohlwill we are convinced that it is a purely degenerative process, and accordingly propose the name "progressive funicular myelopathy, to indicate the character as well as the topographical relationship of the lesions.

The pathologic process is of such a nature that we may predicate the action of a toxin of unknown origin. It is probable that this agent is responsible not only for the changes in the spinal cord and brain, but also for the clinical and pathologic manifestations of pernicious anemia. It seems probable that the degenerative changes in the central nervous system and the changes in the rest of the organism are the joint result of a common factor, rather than related to each other as cause and effect. It is also likely that the same disease process is frequently present in cases in which cord lesions are associated with anemia not pernicious in character. We also feel that the histologic picture in this disease is, in the main, similar to that found by Hassin in multiple sclerosis. In both conditions there is probably an endogenous toxin which has a selective affinity for the myelin. The dissolution of the myelin leads to the exposure of the axis cylinders, which undergo degenerative changes, and are eventually destroyed. This progressive destruction of the parenchyma calls forth a large number of phagocytic elements of glial origin. Side by side with this there occurs a progressive activity of fiber-forming glia cells. The Elzholz bodies are, in our opinion, to be considered as incidental to the destructive changes. Elzholz himself considered them as products of destruction (Abbauproducten) or of myelin metabolism. He did not regard them as specific for degeneration of the axis cylinders. In general the pathologic picture shows a strong similarity to the histologic picture of periaxial neuritis described by Doinikow.[6]

6. Doinikow, Nissl and Alzheimer: Histologische und histopathologische-Arbeiten **4**:445, 1911.

DISCUSSION

Dr. Colin K. Russel, Montreal: Has Dr. Strauss observed in his studies any variation in the severity of the degeneration at the different levels of the same tract? For example, in the pyramidal tract has he noticed that the degeneration in the peripheral part of that tract, in the lower dorsal region, is more marked and more definite than the degeneration of that tract in the pons or in the internal capsule? Or in the posterior columns is the degeneration more marked in the upper cervical than it is in the lumbar region? In other words, has he noticed that the peripheral part of the axis cylinder degenerated before that part approximate to the nerve cell? Such an observation was made by Nageotte, in his work on tabes dorsalis, and it would be interesting to know whether Dr. Strauss' observation confirmed this.

I do not think the suggested change in nomenclature has any advantage over the old term subacute combined sclerosis given by Risien Russell in 1900.

Dr. Lewis J. Pollock, Chicago: Was there any axonal change in the motor ganglion cells? As in central neuritis, in which we have diffuse degeneration of axons, we should expect to find this change in the combined degenerations of the spinal cord.

Dr. George B. Hassin, Chicago: If subacute combined cord degeneration and multiple sclerosis show the same histologic changes, they might be considered as analogous pathologic and clinical entities. There are, however, histopathologic differences. In subacute cord degeneration there are absent the microscopic foci of sclerosis so abundant in multiple sclerosis; the short nerve fibers, especially of the gray matter, are hardly affected in subacute cord degeneration where the long fibers are principally if not exclusively involved. The entire morbid condition in subacute cord degeneration is much more severe and acute than in multiple sclerosis.

I should like to ask Dr. Strauss whether he studied the subarachnoid spaces and the choroid plexus for lipoids?

Dr. Joseph Collins, New York: At the last meeting of the Academy of Medicine in Paris, Dr. August Pettit of the Pasteur Institute demonstrated to the satisfaction of his audience a spirochete which he had been able to transmit to rabbits, mice and monkeys, which caused the typical characteristic lesions of multiple sclerosis.

Dr. Georges Guillian, speaking of this discovery, admitted that he was quite satisfied that the spirochete that had been isolated and with which he had inoculated the animals was undoubtedly the cause of this disease and that it was truly an inflammatory process. Of course, if that is true, there can be no justification for Dr. Hassin's conclusions.

Dr. Henry Viets, Boston: Is there any value in the term "subacute" as used in the title of this paper? Also is not the pathology used by Putnam and Taylor twenty years ago of "diffuse degeneration" the better terminology?

Dr. Adolf Meyer, Baltimore: In the first place, what we had demonstrated to us is not particularly a funicular disease. I think that Dr. Strauss showed the specimen of a section in which the patchy character comes out very well; one part of the funiculus is affected and then farther down it is again involved. Whether it is exactly the same or not, and what the intermediate sections show, I do not know.

It is my conviction (and I think those pictures have shown it again, as have my own specimens) that funiculi are not affected but certain superficial topographical regions, and those rather in a patchy form.

I therefore should not like the term "combined sclerosis" either. There seems to be an autolytic process with secondary reactions that belongs to almost every degenerative process, and therefore multiple sclerosis sections are somewhat similar to this, although in that condition I would perhaps much rather expect myelitic patches with rare destruction of the tissue as such; whereas this seems to me to be an autolysis of tissue in which, of course, various parts of the tissue are unequally resistant. My belief, therefore, is that we deal in multiple sclerosis with patches of various sizes but remarkably circumscribed, capable of involving both gray and white matter irrespective of any funicularity of tissue, whereas in this anemia process, which evidently is much more specifically nutritional, or at any rate in which the metabolism is determined, we have certain usually superficial patches or regions of the spinal cord, far less frequently farther up in the brain stem, in a state of tissue dissolution.

Moreover, from the point of view of symptomatology, the two conditions are so dissimilar that I should consider it rather unfortunate to give the impression of close relation between them.

Dr. Williams B. Cadwalader, Philadelphia: For a long time I have believed that infections or toxins, totally different in nature, are capable of producing lesions in the spinal cord that cannot be differentiated with accuracy by the microscopic appearance alone. If, therefore, we consider the alterations found in the spinal cord associated with severe anemia in this light one might readily find similarities to multiple sclerosis such as Dr. Strauss has shown. But we also know, as Dr. Spiller pointed out at the meeting of the Research Society in 1921, that there is a considerable variation in the appearances of the lesions of multiple sclerosis, depending on the duration of the disease. In a very early stage there are certain changes that Dr. Spiller has shown that appear quite different from those of the advanced stage of the disease. In the combined sclerosis of anemia there are also variations in the appearances of the lesions, depending on the duration of the toxic process. There is a great deal in favor of believing that the process is a toxic one, for occasional cases are found in which the red blood count is normal or nearly so, and yet there is evidence of considerable degeneration in the posterior and lateral columns of the spinal cord. Alterations have been found in the nervous system of certain patients with encephalitis that resemble multiple sclerosis; and the similarity of the lesions of acute anterior poliomyelitis to epidemic encephalitis is well known. In spite of this I do not feel that we are justified in immediately concluding from these facts alone that the diseases are necessarily caused by the same toxin or the same organism. I quite agree with Dr. Meyer that the changes found in combined sclerosis of the spinal cord associated with severe anemia should not be confused with those of multiple sclerosis. The two diseases are in no way related, and are quite different in their clinical aspect as well as their pathology. Minute similarities to which Dr. Strauss has called attention might exist in more than one disease, but they are not discriminating.

Dr. Strauss, in closing: This process has been known by a number of names, none of which has been considered satisfactory. It is true that it does not start with the degeneration of a system, beginning in foci mainly—almost exclusively in the white matter. As these foci grow and coalesce secondary degeneration becomes evident, and if the various foci are large enough and close together there will be a degeneration which might affect an entire column, which might be the terminal system; hence the name "subacute funicular myelopathy."

It is subacute because it is still in progress, and the process takes a number of months and sometimes years. We chose the word "subacute" purposely because in most cases it is in progress.

The cord is more involved than the other parts, the medulla and pons very little. The parts affected are chiefly below the medulla.

It is far from our intention to confuse multiple sclerosis with this disease. We know that the conditions are not alike. We wish to emphasize the fact that the process is a degenerative one and that the picture histologically and anatomically is very similar to that presented in multiple sclerosis. Therefore, if this process can be due to a toxin, it lends support to the view advanced by many that multiple sclerosis is due to a toxin. It is an argument based on similarity of the pathologic and histologic picture.

We did not stain the choroid plexus. The subarachnoid space showed numerous granular cells. We found in one of the cases a thickening of the glia, which Dr. Hassin found in multiple sclerosis and which he regarded as being due to an irritative reaction.

With regard to the pictures shown by us and those shown by Hassin in multiple sclerosis, if they are due to an inflammation, they are seen in no other inflammatory disease that we know of in the central nervous system. Neither poliomyelitis, syphilis nor encephalitis produce a picture similar to this. In those conditions there is a distinct inflammatory reaction. Whether a spirochete is the cause of multiple sclerosis, it is certainly not the cause of funicular myelopathy, for if it were it would be reasonable to suppose that the picture histologically and physiologically would be similar to that which is seen in diseases caused by this organism.

There is only one curious clinical fact that would point to a spirochetal origin of multiple sclerosis, that being the frequency of the colloidal gold reaction in the spinal fluid.

Regarding the resemblance of an acute multiple sclerosis to this, I believe that even the cases of Spiller and similar cases in the literature are either syphilitic or more probably encephalitic.

PAPILLOMA OF THE FOURTH VENTRICLE*

REPORT OF A CASE

ERNEST SACHS, M.D.
ST. LOUIS

A butcher, 50 years old, complained of headache, dizziness and falling on walking. The past history was unimportant. Two and a half years ago he began to have headaches and pain in the lower part of the abdomen. One year ago he had an attack of influenza. During this period his headaches were less severe. During the two months before admission he had intense headaches accompanied by vomiting without nausea and was unable to walk without help. He fell to either side, but most frequently forward. During the past two weeks he had several attacks of unconsciousness lasting from two to ten minutes, unaccompanied by convulsions or twitchings.

The positive findings in the physical examination were: questionable lateral nystagmus to both sides, at times a lateral nystagmus which was quite definite with a slow component to the right, the head held to the right in a cerebellar attitude, hypesthesia of both corneas, more on the right, and normal eyegrounds and visual fields. The visual acuity was: left 20/60, right 20/48. The pupils were equal and reacted to light and accommodation.

There was some cerebellar ataxia, the patient walking with a broad base. When he attempted to stand on either foot he reeled to the right and backward. There was hypotonia of the right leg. There was no adiadokokinesis in either hand; finger to nose test and all tests to determine finer movements of the fingers were normal. There was a history of regurgitation through the nose and difficulty in swallowing. Roentgen-ray examination was negative. Lumbar puncture showed 13 cells, ++ Pandi and a negative Wassermann test. The only abnormalities that the Bárány tests showed were that when the right ear was douched with hot water the patient did not past point with the left hand, when the horizontal canals were tested; when the vertical canals were tested with the patient's head back the patient always past pointed to the left with both hands. Dr. Lyman's comment on these tests was as follows: "The vestibular tests suggest a lesion in the brain stem in the region of the posterior longitudinal bundles. The cerebellum gives practically normal reactions."

---

* Read at the Forty-Eighth Annual Meeting of the American Neurological Association, Washington, D. C., May, 1922.

Fig. 1.—Papilloma of the fourth ventricle removed as shown in Figure 2, under local anaesthesia, through a median line incision. The tumor extended up into the aqueduct of Sylvius. Complete recovery with disappearance of all symptoms.

Fig. 2—Removal of papilloma of fourth ventricle.

The symptoms were so clearly bilateral that it seemed quite probable that the lesion lay in the median line. In view of the occupation of the patient, Dr. Schwab and I both thought of the possibility of a cysticercus infection. The absence of nystagmus suggested that the lesion was superficial and not near the nuclei of the cerebellum. The absence of choked disk suggested that the lesion was growing slowly.

In view of the probable median line location of the process, the usual cross bow cerebellar exposure was not employed; merely a median line incision was made with retraction of the muscles and removal of the occipital bone and the arches of the atlas and axis. This was done under local anesthesia and gave an excellent exposure of the fourth ventricle and the vermis. On opening the dura a white glistening tumor was seen filling the fourth ventricle. This was well encapsulated and was enucleated without much difficulty and without pain to the patient. The tumor extended up into the aqueduct of Sylvius, which was greatly dilated. The only discomfort complained of during the operation was pain in the abdomen. The patient made an uneventful recovery and left the hospital on the eighteenth day after operation. Now, a year after the operation, he is entirely free of symptoms with the exception of slight ataxia when he walks rapidly up stairs.

The three reasons for presenting the case are: 1. The constant pain in the abdomen, which I believed might be interpreted as evidence that there are afferent fibers in the vagus nucleus. This abdominal pain was present both before operation and when the tumor was lifted from the floor of the fourth ventricle. 2. The tumor had completely obstructed the aqueduct of Sylvius and therefore produced an obstructive hydrocephalus, and yet the patient had normal eyegrounds. 3. This case demonstrates the possibility of removing tumors of considerable size in the region of the fourth ventricle through a simple median line incision without freeing the muscles from their attachment to the superior curved line of the occipital bone.

DISCUSSION

DR. FOSTER KENNEDY, New York: Abdominal pain similar to that associated with this tumor is often found in vasovagal attacks, confirmatory evidence of the involvement of the vagus in seizures of that type.

MAGNUS AND DE KLEIJN PHENOMENA IN BRAIN LESIONS OF MAN*

A CONSIDERATION OF THESE AND OTHER FORCED ATTITUDES IN THE SO-CALLED DECEREBRATE MAN

I. LEON MEYERS, M.D.
Attending Neurologist, Los Angeles County and Kaspare Hospitals;
Late Associate Professor of Neurology, University of
Illinois College of Medicine
LOS ANGELES

The phenomena of Magnus and De Kleijn[1] occur with striking regularity and in a pronounced degree in the so-called decerebrate state of both animal and man; that is, in the animal after ablation of both hemispheres of the cerebrum and in man when disease of the cerebrum is of such extent as to eliminate more or less completely its influence on the periphery. In this state the limbs, always the anterior, less constantly the posterior, change posture as a result of passive displacement of the head. These reactions vary with the type of head displacement. They may be bilaterally identical, the limbs on both sides undergoing flexion or extension, or the limbs on one side undergo flexion, while those on the other side undergo extension. The first type of reaction may be one of two: the anterior limbs may flex and the posterior extend or vice versa; or all the extremities may go either into flexion or into extension. When the displacement of the head does not alter its symmetrical relationship to the body, as when flexed directly ventrally or dorsally, the reactions are the same on both sides of the body; the anterior limbs undergoing flexion and the posterior limbs extension in the former instance, the reverse condition occurring in the latter. If the head is rotated, the reactions on one side are the direct opposite of those on the other side—the facial limbs undergoing extension, the occipital limbs flexion. These reactions have been shown by Magnus and De Kleijn to originate in stimuli which arise in the muscles and articular structures of the upper four cervical joints, and have been called by them cervical reflexes. Of these, the type brought about by rotation of the head is generally the most pronounced.

Another type of reaction, called by these observers labyrinthine

---

* Read before the Section on Nervous and Mental Diseases at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Magnus, R., and De Kleijn, A.: Die Abhängigkeit des Tonus der Extremitätanmuskeln von der Kopfstellung, Arch. f. d. ges. Physiol. **145**:455. 1912.

reflexes, is brought about by displacements of the head which change its position in space without altering its position with relation to the body. These reactions, they have shown, originate in labyrinthine impulses. The cervical reflexes are not affected by extirpation of the labyrinths; the labyrinthine reflexes are abolished by this operation. The latter persist if the subject, with labyrinths intact, has its head, neck and thorax so encased in plaster of Paris as effectually to eliminate all movements of the head at the neck, a procedure which makes the appearance of cervical reflexes impossible. The labyrinthine reflexes exhibit themselves in identical change of posture in all the limbs, the anterior as well as the posterior limbs—the latter, however, with less constancy—undergoing either flexion or extension, the type of movement depending on the position of the head with relation to the horizontal level in space.[2] All these reactions are tonic in character; they are reactions of posture, depending on the *position* of the head, not brought about by the movement of the head toward the new position. The reacting limbs are, therefore, maintained in the new position so long as the head remains in its altered position, with the exception of a brief latent period between the displacement of the head and the resulting reaction.

The phenomena of Magnus and De Kleijn being preeminently phenomena of decerebration, are like decerebrate rigidity,[3] of great neurologic interest. These phenomena point to some influence or influences which in the normal state interfere with or render unnecessary their manifestation. What the nature of this influence or these influences may be and what the structural basis is are still mooted questions. The phenomena of Magnus and De Kleijn, as well as decerebrate rigidity, have been correlated by a number of authors with forced movements and forced attitudes. Thus Magnus and De Kleijn [4] interpret the rolling movements of an animal after a unilateral extirpation of the labyrinth as being largely a result of the rotation of the head produced by this lesion, and its consequent asymmetrical reactions in the limbs.

---

2. Magnus, R., and De Kleijn, A.: Arch. f. d. ges. Physiol. **145**:455, 1912; **160**:440, 1914-1915.

3. Sherrington, C. S.: Decerebrate Rigidity and Reflex Coordination of Movements, J. Physiol. **22**:319, 1897; Flexion Reflex of the Limb, Crossed Extension Reflex, and Reflex Stepping and Standing, ibid. **40**:103, 1910; Remarks on the Reflex Mechanism of the Step, Brain **33**:1, 1910; Postural Activity of Muscles and Nerve, ibid. **38**:19, 1915. Integrative Action of the Nervous system, London, Archibald Constable Co., 1908, p. 299.

4. Magnus, R., and De Kleijn, A.: Analyse der Folgezustände einseitiger Labyrinth Extirpation mit besonderer Berücksichtigung der Rolle der tonischen Hals Reflexe, Arch. f. d. ges. Physiol. **157**:238, 1913. Magnus, R., and Van Leeuwen, W. Storm: Die acuten und dauernden Folgen des Ausfalles der tonischen Hals und Labyrinth Reflexe, ibid. **157**:196, 1914.

Rothfeld [5] utilized the Magnus and De Kleijn phenomena in his explanation of the forced movements brought about by stimulation of the labyrinth (by douching or rotation) and the variation in these movements in accordance with the position of the head with relation to the body. The circus movements and falling reactions following such stimulation in animals and the falling reactions and past pointing in man are all, he thinks, evolved from the cervical reactions as described by Magnus and De Kleijn.

Walshe [6] believes that the extended type of spastic paralysis is identical with decerebrate rigidity.

Kinnier Wilson [7] suggests that decerebrate rigidity is responsible for the attitudes in certain tonic fits, occasionally observed in patients with lesions of the midbrain or cerebellum. He extends his theory to embrace the transient positions assumed by the limbs in the movements of chorea and athetosis which, he suggests, are merely fragmentary manifestations of the complete and prolonged decerebrate attitudes.

MAGNUS AND DE KLEIJN' PHENOMENA IN BRAIN LESIONS OF MAN

Magnus and De Kleijn originally observed these cervical and labyrinthine phenomena in the decerebrate animal. In these experiments, the cerebrum is removed by transection of the midbrain at the level of the corpora quadrigemina. They concluded that the same phenomena should be observed, perhaps less fully developed, in man when destruction of the cerebrum is of such extent as to obliterate all its functions. This prediction was verified. They report seven patients,[8] each exhibiting the cervical reactions and two of them the labyrinthine reactions as well. In all of these cases (two necropsies) the cerebral functions were more or less completely abolished, but probably not to the extent attained in the decerebrate animal.

Another case showing the cervical reactions was reported by von Weiland.[9] In this case the patient had an epileptiform attack due to

5. Rothfeld, J.: Ueber den Einfluss der Kopfstellung auf die vestibularen Reactions bewegungen der Tiere, Arch. f. d. ges. Physiol. **159**:607, 1914.

6. Walshe, F. M. R.: The Physiological Significance of the Reflex Phenomena in Spastic Paralysis of the Lower Limbs, Brain **37**:311, 1914-1915; On the Genesis and Physiological Significance of Spasticity and other Disorders of Motor Innervation; with a Consideration of the Functional Relationships of the Pyramidal System, ibid. **42**:1, 1919.

7. Wilson, S. A. Kinnier: On Decerebrate Rigidity in Man and the Occurrence of Tonic Fits, Brain **43**:220, 1920.

8. Magnus, R., and De Kleijn, A.: Ein weiterer Fall von Tonischen "Halsreflexen" beim Menschen, München. med. Wchnschr. No. **46**:2566 (Nov.) 1913; Arch. f. d. ges. Physiol. **160**:429, 1914-1915. Also footnote 1, p. 527.

9. Weiland, Walther, von: München. med. Wchnschr. No. **46**:2539 (Nov.) 1912.

cerebrospinal syphilis and he was in coma. The cervical reflexes were identical with those observed in the decerebrate animal but were limited to the arms. There was no necropsy.

A case showing the typical cervical reflexes is reported also by Kinnier Wilson [7] (Case 14 of his series). Marie and Foix [10] have also reported examples. They state that the reflexes may be observed in ordinary hemiplegia and are brought about by lesions limited to the pyramidal tract system which remove cortical inhibition from the lower centers. The validity of this observation may be questioned. I have looked for these phenomena in numerous cases of recent and old hemiplegia, with and without contractures, and never have found them. According to André-Thomas,[11] he could evoke these phenomena in a number of cases when the brain lesions were severe and extensive (he does not state the nature of the lesions) and when they were associated with intellectual efficiency. This statement is, in a broad sense, borne out by my own observations.

REPORT OF CASES

CASE 1.—*History.*—F. A., a girl, aged 14, was brought to Los Angeles County Hospital on July 10, 1921. Four and a half hours before she had suddenly begun to vomit and soon after that to have generalized convulsions. She quickly passed into coma. The coma and convulsions continued until July 12. The temperature on admission was 103.5 F. It continued to be irregularly elevated until about July 27, when it became normal. The history was obtained from her guardian.

The child was deserted by her parents when she was three years old. Her birth was normal and she was bottle-fed. A brother, a little over a year old, taken care of by the same guardian, suffered from a similar disease. He had paralysis of all limbs and was subject to occasional convulsions. (This brother was brought to the hospital about a month later in a state of coma and convulsions. He died about four hours later before a satisfactory clinical examination could be made. His brain was much larger and generally appeared to be much less diseased than that of the girl. No microscopic examination was made). No data as to the patient's heredity or early infancy were obtained. The child, was never able to sit up; it never made an attempt to walk and never learned to articulate. A year before the biceps femoris of either limb had been transplanted into the patella. Previous to this the child's lower limbs had been rigid with the legs at right angles to the thighs. While at the hospital for this operation she had had an attack of generalized convulsions which lasted for about twenty-four hours.

Examination.—The patient was lying on her back in considerable opisthotonos (Fig. 1); her head retracted and turned so that it was inclined toward the right. With little resistance it could be moved forward, backward and laterally.

---

10. Marie et Foix: Phénomène de Magnus et De Kleyn chez l'homme et mouvements conjugués d'automatisme, Rev. neurol. **28**:120, 1914-1915; Les reflexes d'automatisme dits des defense, ibid. p. 236; Les syncinesies des hemiplegiques, ibid. **30**:145, 1916.

11. André-Thomas: Rev. neurol. **28**:120, 1914-1915. (Discussion.)

All limbs were in spastic paralysis. The lower were in utmost extension with toes pointing down and heels drawn up. They were held rigidly in this position but possessed considerable mobility at all joints. There were markedly increased knee reflexes, ankle clonus and a Babinski sign, more pronounced on the right. The right arm was generally in utmost extension at shoulder and elbow, with abduction at the shoulder, complete flexion and hyperpronation at the wrist and complete flexion of the phalanges. The left arm was generally in abduction and flexion at all its articulations (Fig. 1). These postures of the upper limbs were only the predominant ones—they were not constant, being frequently interrupted, generally at the rate indicated in the tracing (Fig. 2)[11a] by involuntary movements which affected both limbs but the right more markedly. During these involuntary movements the right arm would assume a position of flexion

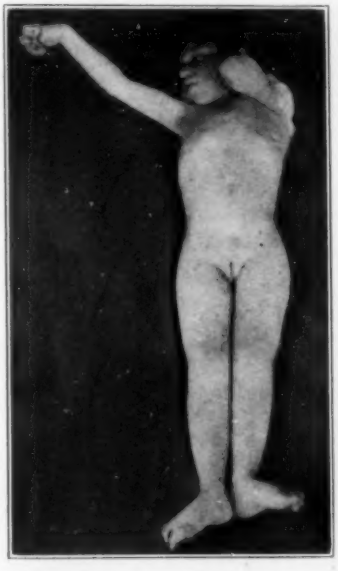

Fig. 1 (Case 1).—Predominant posture of patient.

and adduction or adduction only, and the left a posture markedly similar to the predominant one in the right. The mouth was generally spastically closed. The lower jaw also showed involuntary movements. The mouth would open wide (as in gaping). Some movements of opening and closing the mouth were similar to those occasionally observed in paralysis agitans, but of slower rate and greater range. There were no cranial nerve palsies. Ocular movements were normal, the pupils widely dilated, but they reacted normally to light. There was no nystagmus and the fundi were normal. The patient responded to strong optic and acoustic stimuli fairly well; also to intense stimuli applied to any part of the body, to which she responded by a sharp groan. She appeared

11a. The tracings in Figures 2, 3 and 4 have been obtained by means of Marey's tambours in the manner described in the author's article, The Physiologic Significance of the Babinski Toe Response, Arch. Neurol. & Psychiat. **4**:309 (Sept.) 1920.

to have no difficulty in swallowing. The Wassermann test of the blood and spinal fluid was negative; the fluid was clear, under normal tension and yielded fifteen lymphocytes per cubic millimeter. It showed a trace of globulin.

Mentally, she showed little development. She ordinarily took no notice of surroundings, only occasionally turning her head in the direction of a noise or bright light. She did not cooperate while being fed and understood no commands.

Otologic examination was made by Dr. Isaac H. Jones. Caloric stimulation of the right ear with head back 60 degrees (with water at 68 F.) gave, after eighteen seconds, horizontal nystagmus to the left. The quick component, however, was very sluggish and there was almost persistent conjugate deviation to the right. Caloric stimulation of the left ear gave normal nystagmus to the right. The results indicate a normal condition of the labyrinth but a break somewhere in the cerebral mechanism[12] that is responsible for the quick component in vestibular nystagmus to the left.

The patient exhibited both types of the cervical reactions of Magnus and De Kleijn; that is the type which affects the limbs on the two sides symmetrically and the type which affects them asymmetrically. The reactions occurred exclusively in the upper limbs, possibly because the lower limbs were rather firmly held in complete extension. Thus, when the patient's head was flexed so that the chin was brought almost in contact with the chest, both upper limbs underwent flexion; whereas, if it was sharply retracted, these limbs underwent extension. In either case the arms maintained their position all the time the head remained in its new position (Fig. 3). If the head was rotated, directing the face to one side, the arm toward which the face was directed underwent extension, the other one flexion, the limbs in this case, too, staying in their new position so long as the head remained in its altered relationship to the body (Fig. 4).

That the duration of the new position of the limbs almost always corresponded with that of the head is remarkable in view of the fact that the limbs in the absence of passive displacement of the head were almost continually in motion with involuntary movements of flexion and extension. The reactions were much more pronounced in the right arm than in the left as observed on numerous occasions for about two months following the patient's admission. After that the upper limbs, like the lower, became practically immobile, ultimately assuming an attitude of complete flexion of all segments with gradual diminution and finally disappearance of all reactions. (The patient did not exhibit the labyrinthine reactions of Magnus and De Kleijn. These reactions were also inconstant and little marked in the cases reported by these authors).

Necropsy Examination.—The patient died on Nov. 23, 1921. The necropsy examination performed next day revealed a small cerebrum and a normal-sized cerebellum (Fig. 5). The total water displacement by all the intracranial structures was 470 c. c., by the cerebellum alone 65 c. c. The cerebrum was markedly atrophic in the region of the motor cortex on both sides. In certain areas it gave to touch a sensation of stony hardness. There were no hemorrhagic foci, nor were there any indications of an old meningitis or encephalitis. The

12. Wilson, J. Gordon, and Pike, F. D.: The Effects of Stimulation and Extirpation of the Labyrinth of the Ear, and their Relation to the Motor System, Phil. Tr. Roy. Soc. London, B. **203**:127, 1912; The Mechanism of Labyrinthine Nystagmus and its Modification by Lesions of the Cerebellum and Cerebrum, Arch. Int. Med. **15**:31 (Jan.) 1915.

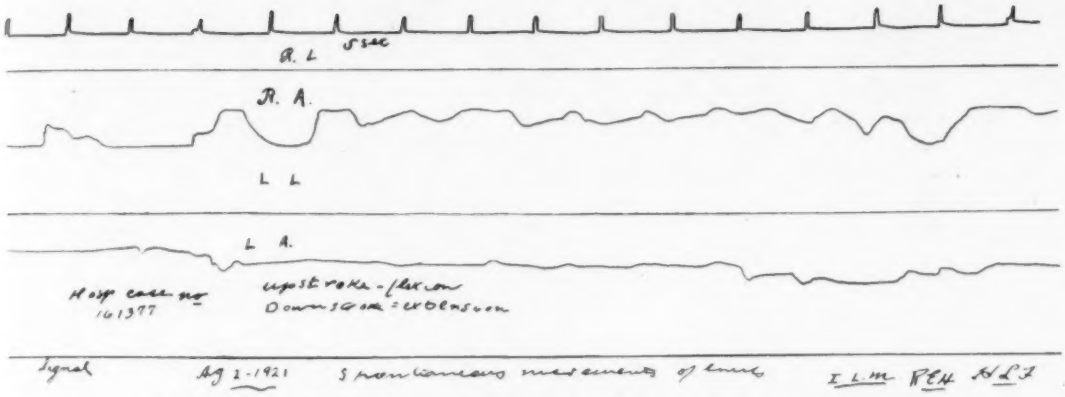

Fig. 2 (Case 1).—Involuntary movements of upper limbs; upstroke represents flexion; downstroke, extension of forearm.

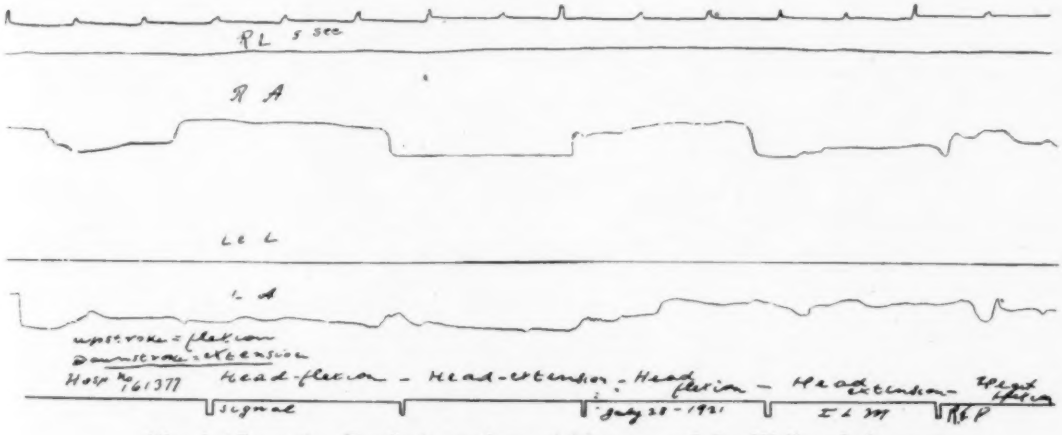

Fig. 3 (Case 1).—Cervical reactions of Magnus and De Kleijn of the symmetrical type. Upstroke represents flexion, downstroke, extension of forearm.

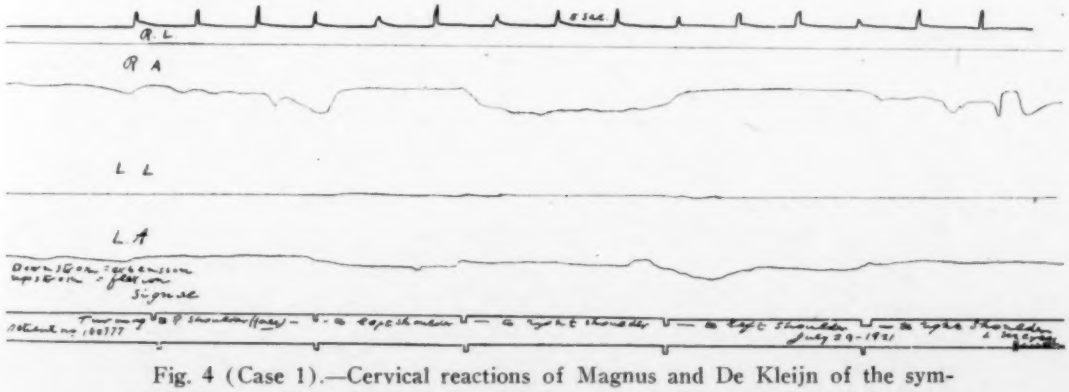

Fig. 4 (Case 1).—Cervical reactions of Magnus and De Kleijn of the symmetrical type. Upstroke represents flexion, downstroke, extension of forearm.

central nervous system was studied microscopically by Dr. George B. Hassin, Chicago. His report follows:

Structures Studied: (1) Spinal cord, (2) cerebellum, including vermis and peduncles, (3) pons, including tegmentum and region of vestibular nuclei, (4) medulla, (5) motor cortex of the cerebrum, (6) right frontal lobe, (7) occipital lobe, (8) island of Reil, (9) cornu ammonis, (10) midbrain structures. Summary of Findings: Secondary degeneration of the pyramidal tracts on both sides throughout the spinal cord (Weigert-Pal stain); degeneration of the motor cortex with secondary proliferative changes in the adventitial and endothelial cells of blood vessels; degeneration of the putamen and globus pallidus (fat accumulation in their ganglion cells and perivascular spaces), normal pons, midbrain (including the nucleus ruber), and cerebellum; frontal and occipital lobes normal; inflammatory changes absent. The degenerative condition, which was confined to the motor cortex and lenticular nuclei, was apparently very severe.

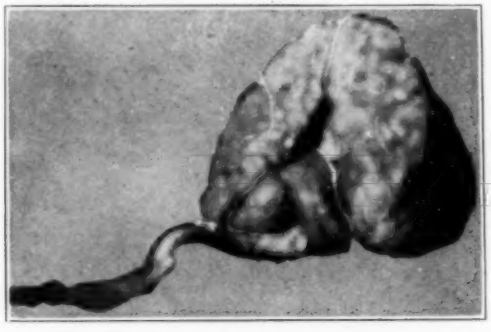

Fig. 5 (Case 1).—Brain of patient.

Another case which exhibited the Magnus and De Kleijn reactions as well as other attitudes of the preceding one, although differing from it in certain particulars, was the following:

Case 2.—*History.*—A Mexican child, 2 years of age, was admitted to the Los Angeles County Hospital on Oct. 5, 1921. The patient was the youngest of three children, all males. The two brothers were normal. The father and mother were well. There was no neuropathic history on either side. The mother had had no other pregnancies. The Wassermann test of her blood was negative. The patient's birth was spontaneous but precipitate. It occurred four days after the mother had recovered from a severe attack of influenza. The child was largely bottle-fed. He was apparently normal, his mother says, until he was 7 months old, when he began to make peculiar involuntary movements with his limbs, chiefly the upper. The child was never able to sit up, to creep or utter a word. His first teeth appeared at 14 months of age. He had measles and, following this, whooping-cough at the age of 19 months.

Examination.—The child was lying on his stomach groaning a good deal of the time. The limbs were spastic in semiflexion (Fig. 6) at the elbows and phalangeal articulations (but not at the wrists) in the case of the upper, and at the hips and knees in the case of the lower limbs. This posture was not constant; it was continually interrupted by involuntary movements of extension.

Fig. 6 (Case 2).—Patient on his back. He is prevented from undergoing "rolling" movements by nurse holding his head in symmetrical relationship to his body.

Fig. 7 (Case 2).—Forced movements affecting his entire body. Note especially the position assumed by the lower limbs and compare this with that of the upper limbs in Figure 1.

These movements were generally of small range but occasionally affected the left lower limb to such an extent as to bring about utmost extension at the hip and knee, utmost plantar flexion with eversion of the foot (so that the dorsum of the foot became directed toward the median line of the body) and the same degree of plantar flexion of the toes. This involuntary movement of the left lower limb was only part of an involuntary movement affecting the entire body. There was extreme retraction of the head, extreme opisthotonos and a movement of complete flexion at all the articulations in the right lower limb (Fig. 7). It will be noted that in this forced movement the attitude of the lower limbs is practically identical with the predominant attitude of the upper limbs in the first case (Fig. 1), the only difference being in the limbs affected. It will be recalled that the predominant posture of the right upper limb was one of extension at the shoulder and elbow, flexion and hyperpronation at the wrist and flexion at the phalangeal articulations. This was, of course, identical with the extension at the hip and knee, plantar flexion with eversion of the foot and complete flexion at the phalangeal articulations in the left lower limb of the second patient. The contralateral limbs in either case were during these forced movements in complete flexion at all their

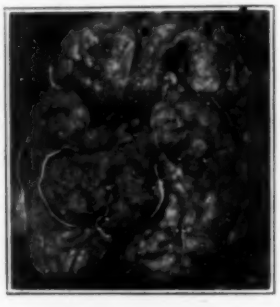

Fig. 8 (Case 2).—Brain of patient.

articulations. The patient was unable to be on his back for longer than a few minutes, as he invariably turned around so as to lie on his stomach, the rotation taking place most generally toward his left side, but occasionally toward his right. In this rotation the head led, the trunk following it. Such a rotation around the longitudinal axis, while observed with great frequency in experimental lesions of the eighth nerve and occasionally in lesions of the cerebellum, is rarely seen in man. It was observed by Stewart and Holmes in only one of their forty cases of cerebellar tumor.[13] These rolling movements in this patient could be effectually stopped by holding his head immobile in the median line (Fig. 7). This is in accord with the observations of Magnus and Van Leeuwen[14] in the case of the rolloing movements in animals following unilateral extirpation of the labyrinth.

While the patient was in the sustained muscular spasm which held him in the attitude described, none of his tendon reflexes could be obtained and it

13. Stewart, T. G., and Holmes, Gordon: Symptomatology of Cerebellar Tumors; Study of Forty Cases, Brain **27**:525, 1904.

14. Magnus, R., and Van Leeuwen, W. Storm: Arch. f. d. ges. Physiol. **157**:196, 1914.

was difficult to obtain any response to plantar stimulation, but the abdominal reflexes were present. In order to bring about relaxation of this muscular spasm, the patient was kept in a warm bath for a little over an hour. It was then noted that his tendon reflexes were normal, that he had no ankle clonus, and that his plantar response was flexor in type. At the same time it was found that he exhibited the cervical reaction of both types; that is the type produced by ventral or dorsal flexion of the head and affecting the limbs on the two sides symmetrically, as well as the type which results from rotation of the head and affects the limbs asymmetrically. This examination following relaxation induced by a prolonged warm bath was repeated several

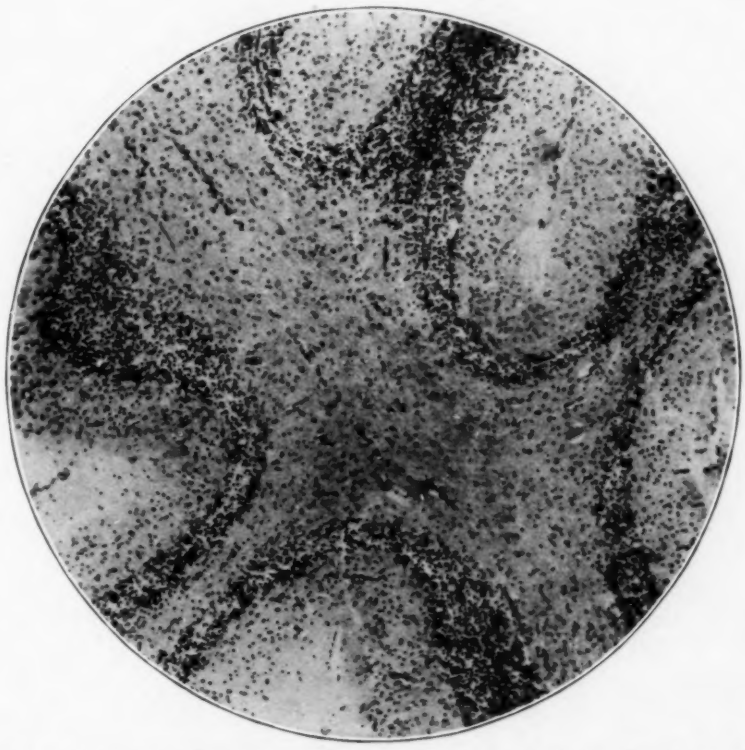

Fig. 9 (Case 2).—Herxheimer scarlet red stain; X 230. Marked and extensive degeneration of ganglion cells which are replaced by fat.

weeks later with the same results. The rotation of the head to one side or the other for the purpose of eliciting the asymmetrical reaction was, however, quickly followed by movements of rotation of his entire body.

The patient showed no cranial nerve palsies, his pupils were equal and reacted well to light. There was no nystagmus, and the fundi were normal. He showed no Trousseau, Chvostek or Erb phenomenon. The muscles showed no atrophy and responded normally to electricity. Mentally, he was in the same condition as the first patient. He could not sit up, he made no attempt to articulate and did not cooperate while being fed.

An otologic examination by Dr. Isaac H. Jones revealed: Turning to the right, head 30 degrees forward (child held in proper position by an adult

who revolved with him) yielded horizontal nystagmus to the left, very large amplitude and very slow, duration twenty-five seconds. After turning to the left a similar large slow nystagmus to the right was obtained. After douching the left ear, there occurred after thirty seconds conjugate deviation of the eyes to the left, then horizontal nystagmus to the right, then back again to conjugate deviation to the left. In douching the right ear there occurred after thirty seconds horizontal nystagmus to the left and then a tendency to conjugate deviation of the eyes to the right. Vestibular stimulation thus showed vestibular responses but some interference with the quick component, the eyes

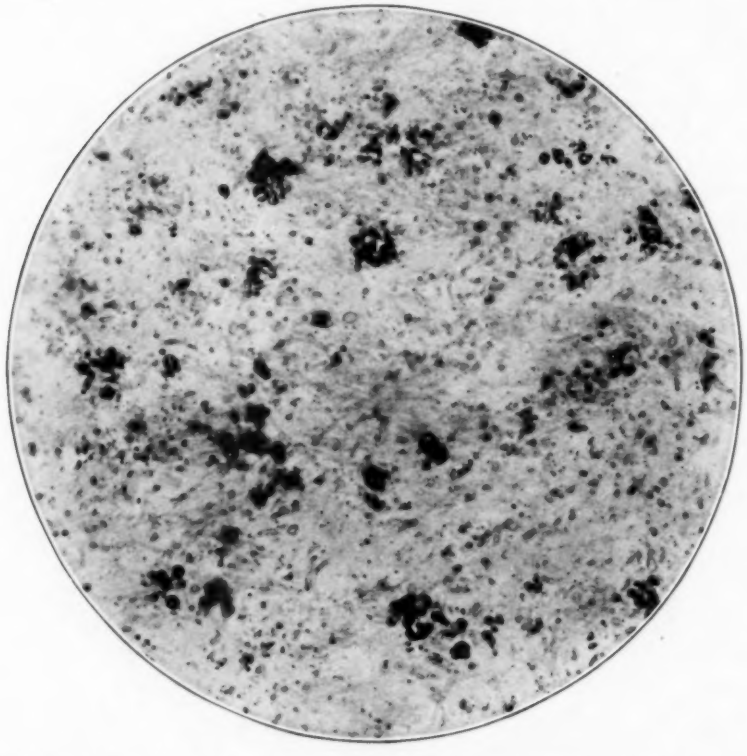

Fig. 10 (Case 2).—Upper vermis of cerebellum. The granular layer of the cerebellum is markedly rarefied and atrophied. The numerous black spots are glia cells. Thionin stain, X 60.

having a tendency to persist in conjugate deviation. The child showed in addition absence of constitutional responses to such stimulation. There was no pallor, no sweating, no nausea.

Necropsy Examination.—The patient died on Oct. 29, 1921. The brain gave a water displacement by all the intracranial structures of 730 c. c.; by the cerebellum alone of only 30 c.c. Macroscopically, the cerebrum showed no atrophies, no scars and no hemorrhagic foci. The cerebellum, on the other hand, was markedly atrophic, and aside from its small relative size, the left hemisphere was much narrower and generally smaller than the right (Fig. 8). The central nervous system was studied microscopically by Dr. George B. Hassin.

The structures studied were: (1) nuclei of the seventh and eighth nerves; (2) cerebellum, including the vermis; (3) peduncles, including the nucleus ruber; (4) medulla; (5) lenticular nuclei; (6) island of Reil; (7) right frontal lobe; (8) left temporal lobe; (9) left motor cortex, and (10) right occipital lobe. His findings were: absence of secondary degeneration of the spinal cord; normal medulla and pons. The nucleus ruber showed in silver specimens no particular change in the glia cells. The putamen and nucleus caudatus were practically normal in contrast to the globus pallidus which showed an abundance of fat (Fig. 9). The motor cortex showed no degenerative changes; the cerebellum showed preserved Purkinje cells but a rarified, actually atrophied granual layer (Fig. 10).

THE PATHOGENESIS OF THE CLINICAL MANIFESTATIONS IN THESE TWO CASES

In studying the clinical phenomena here reported in their relationship to the pathologic findings, we note first that whereas some of the phenomena were common to both patients, others were peculiar to each. Of the latter variety were the "rolling" movements of the second patient. These were undoubtedly due to the cerebellar atrophy which was quite extensive and generalized. That the vestibular system was apparently intact throughout its entire course, i. e., beginning in the labyrinth up to and including its connection with the nucleus of the sixth and third nerves as shown, clinically, by the presence and normal direction of the nystagmus on vestibular stimulation and anatomically by the absence of any lesions in the medulla or pons, is noteworthy. It tends to show that lesions limited to the cerebellum and not involving the vestibular system are capable of producing this type of forced movements. This, as well as the direction of the movements, which in the case of this patient occurred mostly toward his left side, in the direction of the cerebellar hemisphere most affected by the atrophy, are subjects of considerable controversy and have not as yet been definitely settled.[15]

The phenomena which were exhibited exclusively by the first patient were those that are dependent on destruction of the pyramidal tract system; namely, the exaggerated tendon reflexes, ankle clonus, Babinski sign and absence of abdominal reflexes.

Both patients were markedly spastic. In the first patient it ultimately fixed the segments so that all involuntary movement became impossible. In the second patient it produced a state of semiflexion only, allowing slight involuntary movements at all times, and occasionally also of such extreme degree as shown in Figures 1 and 6. The latter type of spasticity, with involuntary movements of varying degree,

15. Muskens, L. J. J.: An Anatomico-Physiological Study of the Posterior Longitudinal Bundle in its Relation to Forced Movements, Brain **36**:352, 1914. Meyers, I. Leon: Galvanometric Studies of the Cerebellar Function, J. A. M. A. **65**:1348 (Oct. 16) 1915.

has been noted also in the striate syndromes described by C. and O. Vogt.[16] It was present in association with involuntary movements of the tremor variety in the cases of progressive lenticular degeneration reported by Kinnier Wilson,[17] which, as in my second case, showed clinically, no exaggerated reflexes, no ankle clonus and no Babinski sign; and pathologically, absence of motor cortex and pyramidal tract affection. The spasticity in this type of cases, i. e., in lesions of the striate system, is difficult of interpretation.[6, 10]

Other phenomena exhibited by both patients were the reflex and spontaneous attitudes of decerebration; the first, as represented by the cervical reflexes of Magnus and De Kleijn; the latter, by the involuntary movements of the body as well as of the limbs. The attitudes assumed by these patients in some of the involuntary movements were, I think, incomplete attitudes of decerebrate rigidity. The extension of the upper limbs at shoulders and elbow, the flexion of wrist and hyperpronation—flexion of the phalanges, as seen in the right upper limb, in the first case, practically the same attitude of the left lower limb in the second case, retraction of the head, opisthotonos and spastic closure of the mouth, are features which are so characteristic of the decerebrate state as to lead us unavoidably to this conclusion. The attitudes assumed by either of our patients were transient only, never so persistent as in the decerebrate animal. Probably this is because the lesion responsible for the attitudes was not so complete as in the experimental animal submitted to transection of the midbrain.

It should be noted that the second patient exhibited the decerebrate attitudes regardless of the cerebellar atrophy. This is in accord with the observations of Sherrington,[3] Thiele,[18] and Magnus [19] that removal of the cerebellum in animals does not diminish decerebrate rigidity. Both patients exhibited also a tendency to persistent conjugate deviation of the eyes on vestibular stimulation—impairment of the quick component of the nystagmus. This component, experimental evidence shows, is a corrective movement for the purpose of restoring the eyes to their normal position following their displacement while in conjugate deviation, and is cerebral in origin. Its impairment is, therefore, to be interpreted as indicating a disturbance of this cerebral function. Finally, neither patient could sit up, move about or articulate, an incapacity far greater than could be accounted for by the spasticity.

---

16. Vogt, Cecile, and Oskar: Zur Lehre der Erkrankungen der Striären Systems, J. Physiol. u. Neurol. **25**:631, 1920.

17. Wilson, S. A. Kinnier: Progressive Lenticular Degeneration, Brain **34**: 295, 1912.

18. Thiele, F. H.: On the Efferent Relationship of the Optic Thalamus and Deiters' Nucleus to the Spinal Cord, J. Physiol. **32**:355, 1905.

19. Magnus, R.: Arch. f. d. ges. Physiol. **157**:225, 1914.

The fact that these symptoms were common to both patients and that the only important lesion common to both was degeneration in the lenticular zone, leads us to conclude that it was this lesion that formed the basis for these phenomena. The fact that in these cases the pathologic process was congenital and set in before the ganglion cells and their conducting fibers had the opportunity to mature may account for the extreme severity of their various clinical manifestations.

THE PHYSIOLOGIC INTERPRETATION OF THE DECEREBRATE ATTITUDES

Magnus and De Kleijn [1] interpreted the cervical reactions of the decerebrate animal as components of certain normal attitudes, attitudes which are inaugurated by movements of the head but which affect the entire body. Thus, when a normal cat drinks milk from a cup on the floor, in lowering her head, she flexes the fore-limbs and extends the hind-limbs to facilitate the approach of her head to the cup. She makes just the reverse movements with the limbs when she elevates the head to seize a piece of meat above her. An animal extends the limbs on the side toward which the face is directed when gazing around to one side or the other. In the decerebrate animal, according to this view, the limbs assume postures in response to passive displacements of the head corresponding to their movements caused by active or voluntary displacement in the normal animal.

This is also the explanation of Marie and Foix,[10] who designate them associated movements of the coordinative type (syncinésie de coordination), and ascribe them to the automatic activity of the lower centers (l'automatisme medullaire).

The conclusion is that these phenomena occur only in the presence of exalted spinal automatism, which is produced only by a very severe cerebral lesion, a lesion involving the lenticular zone and especially the phylogenetically older part of it, the paleostriatum.

As regards the phenomena constituting decerebrate rigidity, Sherrington [20] believes that they represent the postural reflex of standing. "Standing appears to be the functional meaning of the rigidity." The decerebrate animal is capable of maintaining its balance when on its feet; when placed on the ground "it stands," whereas the spinal animal cannot do so. The decerebrate rigidity is, according to this conception, produced by the sustained and extreme contraction of those muscles which oppose the force of gravity, tending to pull the body or its various parts down. The rigidity, in other words, is the expression of the unrestrained activity of one of the two systems of motor innervation, which are postulated by him in accordance with the teachings of Hughlings Jackson, namely, the tonic system, situated in the midbrain or hindbrain. This system, in accordance with his theory, innervates

20. Sherrington, C. S.: J. Physiol. **40**:107, 1910.

predominantly the extensors or antigravity muscles, thus subserving the maintenance of the standing posture, the "continuous movements" of Hughlings Jackson, as opposed to the other system, represented by the phasic centers in the cerebrum which by subserving the "changing movements" of Jackson innervate predominantly the flexors.

"There can be no doubt," says Kinnier Wilson, an adherent of this theory, "that decerebrate rigidity is a release phenomenon, and that a lower influx invades what a higher abandons." This theory is open to certain objections. In the first place, the decerebrate attitude is not one of standing. Postures are assumed in this attitude by various parts of the body which do not in any way form components of the normal standing. The head is retracted, the back opisthotonic, the tail elevated, the mouth rigidly closed and the toes, occasionally also the hand or paw, flexed. One gets the impression that the capacity of the decerebrate animal to "stand" is but an inevitable accompaniment of its attitude, and not the primary purpose of the attitude. Second, it is difficult to conceive of a neuromuscular mechanism differentiated for special activities, local or postural. All the physiologic evidence available tends to show that all motor activity, whether originating in brain or spinal cord, is directed toward the accomplishment of certain purposive movements,[21] and this is probably uninfluenced by the type of movement, whether it is to subserve posture or not, and the kind of muscles, antigravity or others, that are required for the purpose. I should, therefore, like to suggest that the decerebrate attitudes are compensatory, adopted by the animal (or man) as a protective measure following the loss of its cerebrum, and consequently the faculty by which it is enabled to correct deleterious muscular displacements. This capacity to correct muscular maladjustment, either for maintaining the body equilibrium or for the proper execution of other movements, appears to be possessed chiefly by the cerebrum; in the higher animals probably exclusively by this organ. The integrity of this organ, as pointed out in the foregoing, is essential for the correction of the conjugate deviation of the eyes which results from stimulation of the labyrinth. It is also essential, as shown by Muller and Weed,[22] for the rotation of an animal, when dropped from a height with its feet up. The decerebrate animal under such circumstances falls on the back, side, etc. It makes no attempt to correct its position in space in order to alight on its feet. This cerebral faculty is lost, it appears from the pathologic evidence in the cases here reported, by a lesion

21. Beevor, Charles E.: Muscular Movements and their Representation in the Central Nervous System. London, Adlard and Son, 1904, p. 77.

22. Muller, Henry R., and Weed, Lewis H.: Notes on the Falling Reflex of Cats, Am. J. Physiol. **40**:377, 1916.

of the lenticular zone, and especially its pallidal portion. That the corpus striatum, and especially the pallidal portion (the paleostriatum of Edinger) is, as shown by the anatomic studies of Arien Kappers, de Vries, and others,[23] both an afferent and efferent structure, makes the loss of this faculty in lesions of this organ intelligible either on the assumption that it is a sensory function, an expression of sensory impressions and conscious knowledge of position, or that it is a purely motor function and dependent on a normal efferent mechanism and an appropriate motor innervation of the body musculature. The attitude of decerebrate rigidity represents, then, a biologic reaction by means of which the animal seeks to prevent its displacement as a whole or in part by the continuous environmental stimuli, displacements which the animal in the absence of the cerebrum is incapable of correcting. The reaction consists of powerful contraction of the strongest muscles of the body: the retractors of the head, the erectors of the spine, the elevators of the lower jaw, the extensors of the shoulder and elbow, the pronators of the forearm and flexors of the phalanges in the case of the upper limbs, and the extensors of the hip and knee, the envertors and extensors of the foot[24] and the flexors of the phalanges of the lower limbs. In this way the animal offers its maximum of resistance to such external forces as might bring about malpositions in various parts of its body. This reaction originates in the vestibular nuclei of the pons. Their integrity is essential for this phenomenon. Section of the medulla below these structures is not followed by rigidity (Sherrington and Thiele), and this operation in the decerebrate preparation abolishes the rigidity already developed.

Such compensatory reaction by one part of the central nervous system, following the loss of another, is not unknown in neurology. The patient with a cerebellar tumor rotates his trunk so that the shoulder on the side of the lesion is held in front and higher than the contralateral shoulder in order to prevent his walking in a circle,[13] the cerebrum compensating the loss of cerebellar activity. The tabetic patient propels his foot violently forward in order to make sure that it is elevated above the ground, etc.

If this theory is correct, the decerebrate attitudes, the impairment of the quick component of nystagmus and the inability to sit up, to creep and to articulate, as exhibited by both of my patients, are not independent phenomena, but manifestations of one fundamental disturbance; namely, the loss of capacity to bring the muscles into harmonious relationship for the execution of voluntary and purposive

23. Wilson, S. A. Kinnier: An Experimental Research into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:479, 1914.

24. Duchenne, G. B.: Physiologic des Mouvements, Paris, 1867.

movements and to correct such maladjustments as are continually brought about in the body by the incessant activity of the environmental stimuli.

718 Brockman Building.

DISCUSSION

DR. MARY FREEMAN, Perrine, Fla.: Is the cause of this condition known?

Dr. I. Leon Meyers, Los Angeles: The cause is unknown. It appears to be a primary degeneration. In the case of the girl we do not know the family history as the patient was a deserted child, but the fact that the brother also suffered the same trouble would indicate agenesia or lack of development.

DIAGNOSTIC VALUE OF BLOOD SUGAR CURVES IN NEUROLOGY*

SIDNEY I. SCHWAB, M.D.

ST. LOUIS

This study was begun with the idea of ascertaining whether characteristic sugar curves were found in instances of suspected glandular anomalies, for the purpose of differentiating one type from another through the curve characteristics. The only thing of value discovered was a low sugar curve and an increased tolerance in some cases in which dysfunction of the pituitary was evident. In such instances the diagnostic value of the curve was of little importance when contrasted with other symptoms and findings. As this work went on it became evident that some other factor was present which produced curves of a distinctly abnormal kind in cases which showed no clinical evidence of glandular dysfunction. This element by exclusion was thought to be some kind of mental anomaly associated with or originating from emotional abnormality. Of particular importance in this early series of cases were states of anxiety, fear, apprehension, repression and conditions to which the term depression was given. In many instances a high sugar curve was found. There was nothing in cases of this kind to cause a deviation from the normal except the mental state. General and neurologic findings in these patients were uniformly negative. The curves were tabulated as a possible aid in differential diagnosis. About this time F. H. Kooys' article on "Hyperglycemia in Mental Disorders" came to my attention. The significant point in this paper is the conclusion that the emotional state is responsible for the altered types of curves, no matter what particular type of disease the patient clinically presents. This conclusion appeared to confirm the observations made in our early preliminary series.

The study of sugar curves was then extended for the purpose of answering several questions naturally arising:

1. Are characteristic types of curves found in certain diseases and not in others?
2. Have these curves any diagnostic value?
3. Is emotion in a broad sense the factor of consequence?
4. Are sugar tolerance studies of sufficient value neurologically to make the procedure routine in all cases?
5. Have blood sugar curves any prognostic or therapeutic value?
6. What physiologic and chemical mechanism produces such curves?

---

* Read at the Forty-Eighth Annual Meeting of the American Neurological Association, Washington, D. C., May, 1922.

In order to answer these questions an unselected series of neuropsychiatric cases were studied in reference to sugar tolerance curves. From these were excluded those in which sugar values might be influenced by other than neurologic factors. Diabetes, acute infectious diseases, thyroid abnormalities, gastro-intestinal diseases, hypertension, etc., were excluded. About 150 instances fell in the category of primary neurologic cases, and these form the material on which this study is based. An analysis of this material shows that it includes all the ordinary neuropsychiatric diseases such as might be admitted into the neurologic service of a general hospital. Thirty-eight were frankly psychoses; that is, cases in which the mental symptoms dominated the picture. The neuroses are next in number; then come epilepsies, brain

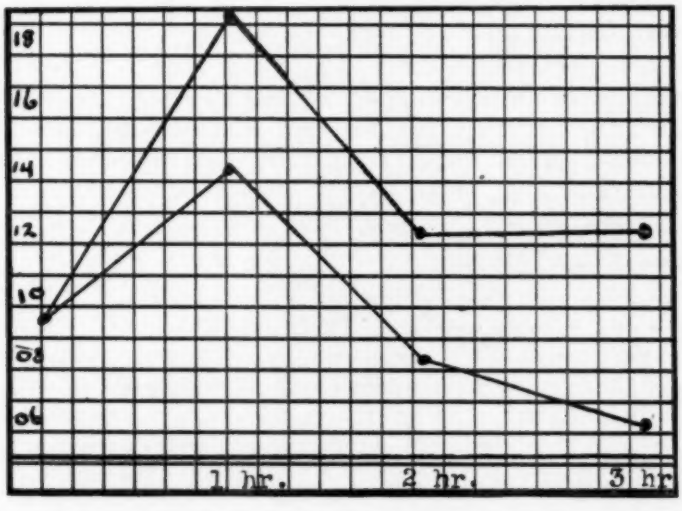

Chart 1.—Normal blood sugar curves preceded by twelve hours of fasting; findings given at the end of one, two and three hours.

tumors, cerebrospinal syphilis, encephalitis and other types of organic nervous diseases. These cases were all studied under hospital conditions and were put through the neurologic routine usual in the neurologic service of the Barnes Hospital. The laboratory work was carried out under the direction of Dr. Olmstead, head of the metabolic ward of the hospital. This work was done under exactly the same conditions, so far as technic was concerned, as was used in the study of a series of cases published by him recently under the title of "A Study of Blood Sugar Curves Following a Standardized Glucose Meal." This paper is referred to for the laboratory technic and methods. Attention should be called to the fact that in this series of cases two methods of sugar determination were used—Meyers and Bailey's modification

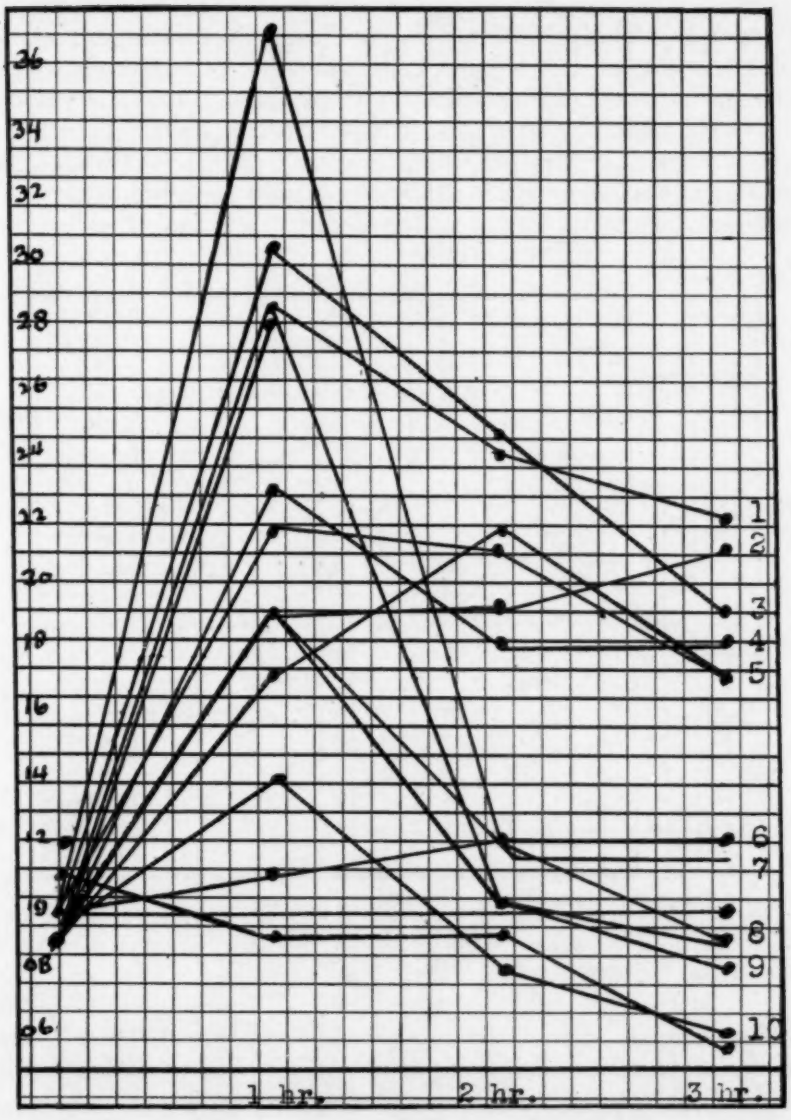

Chart 2.—Blood sugar curves from a group of patients with psychoses after twelve hours of fasting. 1, manic-depressive cases; 2 and 6, dementia praecox; 3, toxic disorientation; 4, psychosis (hallucinosis); 5, senile psychosis; 7, deterioration; 8, depression (paranoid); 9, organic dementia; 10, depressed state (suicidal).

of the Benedict and the Hartman-Schaffer; one is a calorimetric and the other a trituration—an iodometric. Although there is a difference in the amount of sugar percentage obtained, the Hartman-Schaffer giving a consistently higher value, the characteristics of the curve are not altered. The typing of curves, therefore, can be used without reference to the technic employed. In the series of cases here studied a normal curve was first obtained as a laboratory standard and a clinical control by the study of five normal persons and a series of about forty patients in the hospital who showed no demonstrable cause for disturbed glycogenic function. These curves agree with those of

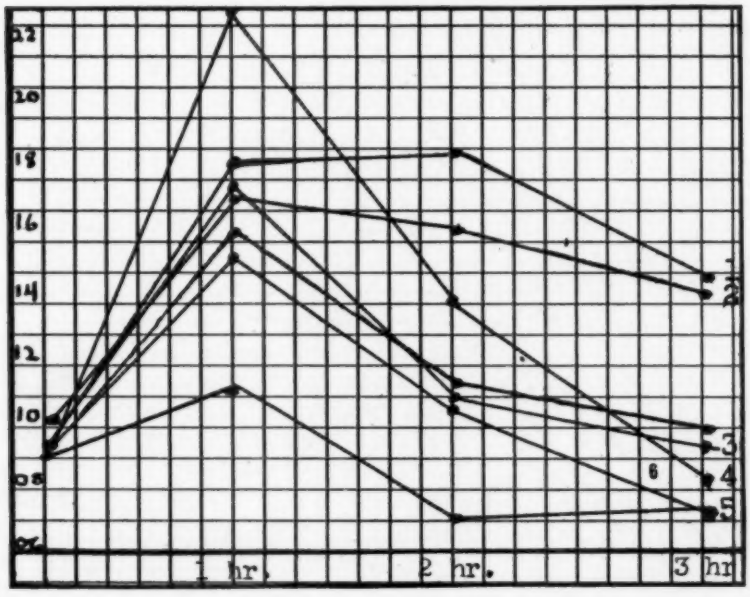

Chart 3.—Blood sugar curves from a group of patients with neuroses after twelve hours of fasting. 1, 4 and 5, hypochondriasis; 2, psychasthenia; 3, neurasthenia; 6, hysteria.

other observers. Figures for the normal curve are as follows: After a twelve hour fasting period the blood sugar shows a variation from 0.09 to 0.1; after one hour from 0.14 to 0.19; after the second hour from 0.08 to 0.12; after the third hour from 0.06 to 0.12 per cent. All curves which deviated in any considerable manner from these normals were regarded as atypical. In the study of abnormal types of curves particular attention was directed to two variations. First the high sugar content after the first hour; second, the sustained elevated curve and the low sugar value throughout the three hours. These represent the three extremes on which a diagnostic value might

be based. The initial hyperglycemia after fasting was considered of physiologic interest only, as was its opposite—a low one; that is, a hypoglycemia. Minor variations of all sorts which altered the normal appearance of the curves were not taken into consideration.

In the group of the psychoses twenty out of thirty-eight cases showed distinctly abnormal curves. These were shown by two things —an initial rise far beyond the normal and a sustained rise beyond

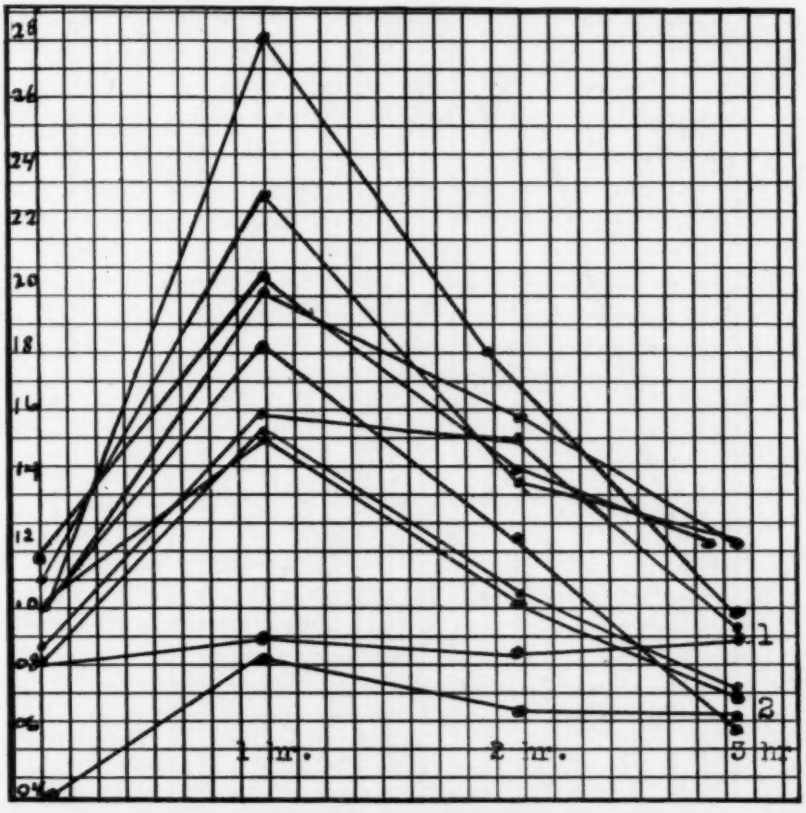

Chart 4.—Blood sugar curves from a group of patients with epilepsy after twelve hours of fasting. 1, postepileptic stupor; 2, pituitary disorder.

the second hour and often no return to the normal level. It is sugnificant that the type of curve had absolutely no relation to the clinical picture presented; that is, there was no curve which might be said to represent, for example, dementia praecox, or manic depression, or any other condition. The patients who presented clinically a dull, apathetic. anxious, or depressed state seemed to show on the whole the most definite sugar value deviations. No diagnostic value other than this could be obtained.

In the neuroses group of twenty-five cases few abnormal curves were found. Six curves were definitely considered abnormal; two of these should be excluded on account of complicating factors. Of the three remaining, two were in marked cases of hypochondriasis in which the anxiety elements were pronounced. This is of some interest as it supports what has been previously pointed out—that of all the neuroses this type approaches more nearly a psychosis in mechanism.

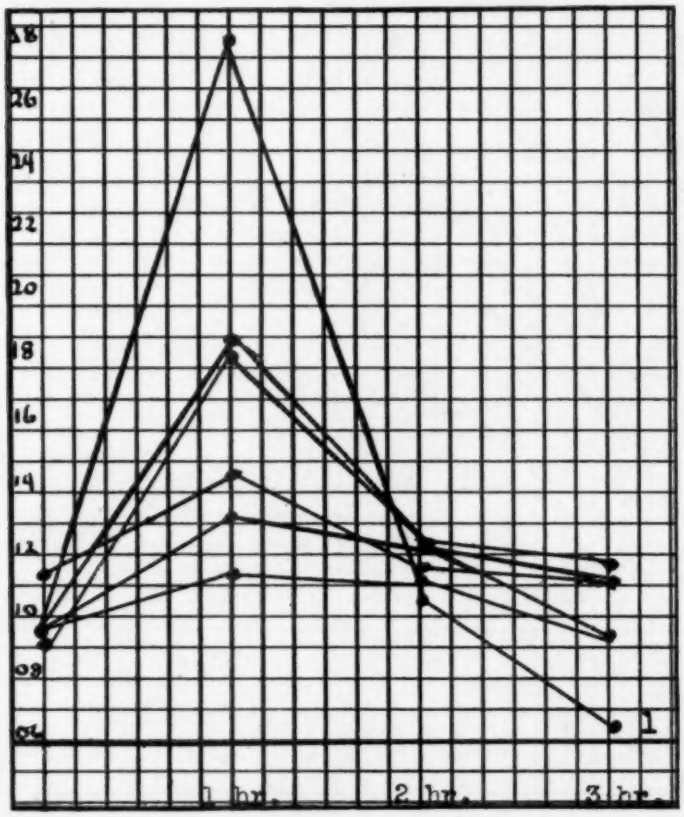

Chart 5.—Blood sugar curves from a group of cerebral tumors after twelve hours of fasting. 1, mental symptoms.

Practically no case of hysteria showed any abnormal curves. In the group of patients with syphilis of the nervous system no abnormal curves were found except in instances in which definite psychotic symptoms were present. The group with paresis showed no abnormal curves. In almost all forms of epilepsy the curves were normal, with the exception of one or two instances in which there were marked mental symptoms. The curves in cases of brain tumor, other than the two instances

in which there was evidence of mental symptoms, were normal. The remaining cases of organic nervous disease cannot be classified in respect to curves. They showed nothing that could be in any way connected with the particular disease in question.

Certain conclusions are fairly obvious, and I believe that the series itself is comprehensive enough to give a broad point of view on which the value of this procedure might be based. The abnormal types of sugar curves were found chiefly in the psychoses. Their occurrence in the neuroses is too uncertain and too scattered to be seriously considered. Organic diseases of themselves do not affect the sugar mechanism sufficiently to alter the curve value; if it is affected, an additional factor has entered into the case. Whenever anomalous curves are

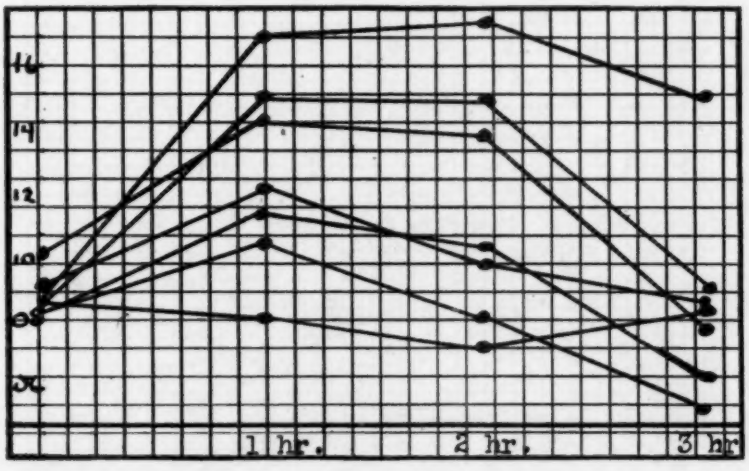

Chart 6.—Blood sugar curves from a group of patients with epidemic encephalitis after twelve hours of fasting.

found outside of the psychoses there is evidence also of an abnormal mental state, usually one in which there is no adequate muscular outlet. States in which there is a good deal of excitement or restlessness do not show an abnormally high curve. Unusually excited patients are not included in this series, as they are not commonly admitted to the neurologic service at the Barnes Hospital. The low curves seen in hypopituitarism or hypothyroidism are of little significance in material such as this, because the neurologic symptoms here present are not primary. The participation of these glands, as well as of the thyroid gland, in abnormal mental states is a matter in which so much confusion of opinion exists at the present time that no adequate conclusion can be formed

It is believed as a result of a consideration of these curves that it is impossible to attach characteristic types of curves to one type of disease. This refers to the psychoses as well as to other types of nervous and mental disease; that is, there is no specific diagnostic value in any one type of curve. The most that can be said is that the group of psychoses as a whole shows by far the largest percentage of abnormal curves, and that in other diseases of the nervous system, whether

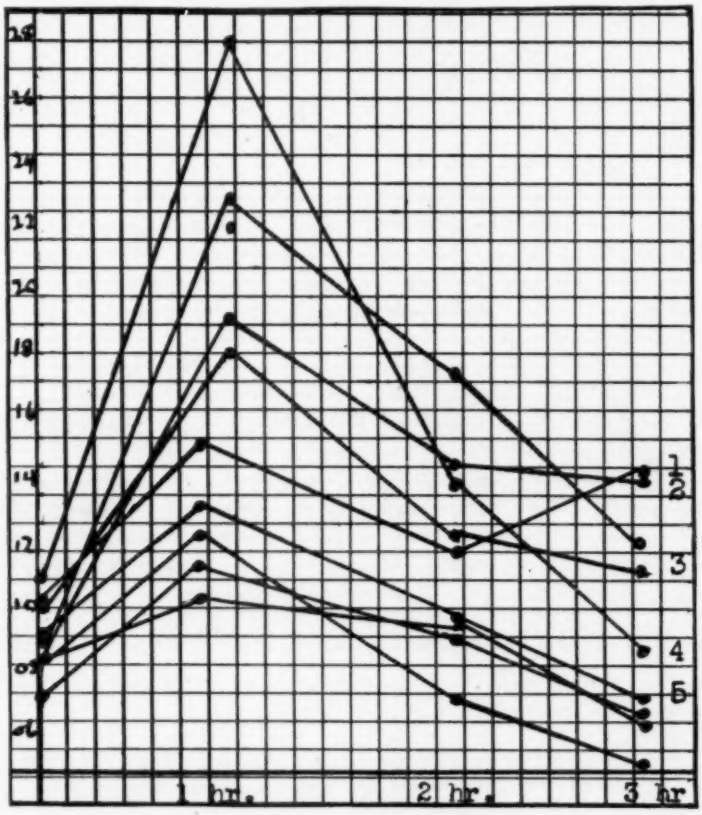

Chart 7.—Blood sugar curves from a group of patients with cerebrospinal syphilis after twelve hours of fasting. 1, dementia praecox; 2, 4 and 5, paresis; 3, tabes.

organic or not, in which atypical curves are found, the most reasonable causative factor seems to lie in the kind of mental reaction that is present.

Sugar curves have no important differential diagnostic value. The one factor that seems to stand out as a causation in the modification of sugar curves is emotion, or rather in a broad sense, the emotional factor in the patient's abnormal mental processes; that is, states of

primary depression, anxiety, apathy, unconscious conflict processes appear to be the states in which high sugar curves are almost universally found. The purely intellectual defects, such as are seen in paranoid states, do not seem to produce abnormal types of curves. On the whole it might be said that deteriorating processes or secondary dementing processes do not of themselves cause abnormal sugar values in the blood.

Sugar tolerance studies are not believed to be of sufficient value neurologically to make this procedure routine in all cases. The whole technic is difficult to carry out; it is time consuming, often disagreeable to the patient. Therefore, cases should be selected in which the type of sugar curve might prove of some value. Just what this value might be is somewhat difficult to say at the present time, but it is possible

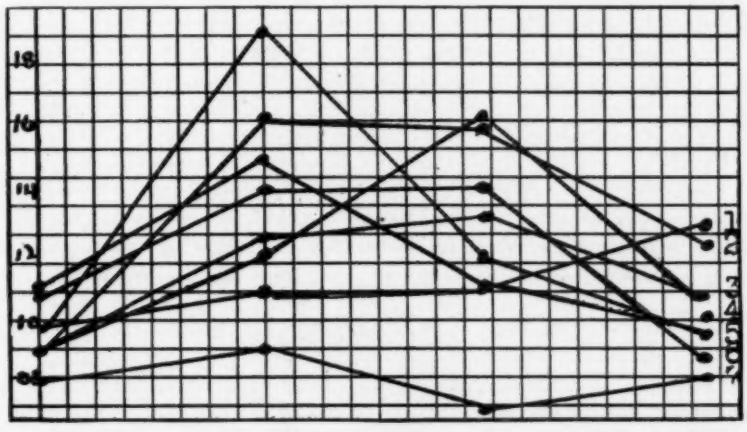

Chart 8.—Blood sugar curves in a group of patients with miscellaneous diseases of the nervous system after twelve hours of fasting. 1, arteriosclerosis (pontile hemorrhage); 2, Meniere's disease (otitis hemorrhagica); 3, neuritis; 4, cerebral hemorrhage, paralysis agitans; 5, dystrophy muscularis; 6, old hemiplegia; 7, trigeminal neuralgia.

that it might be used in differentiating cases in which it is important to find out whether the whole picture is primarily an emotional one or in which the emotional reaction is purely secondary. This would refer particularly to the neuroses in which the patient is in a borderland between neuroses and psychoses. Even here the value of this procedure might be questioned.

Blood sugar curves have no prognostic value, and their change in type cannot at the present time be interpreted as a proof of the effectiveness of therapeutic procedures.

The physiologic and chemical mechanism involved in the production of these abnormal curves is still a matter of debate. The theories

which have been advanced to explain them revolve chiefly around the original ideas of Cannon as a result of the various experimental studies on emotional glycosuria. The chemical factor that has shown the most definite causative influence is the increase in epinephrin. Even this fact has been disputed. The biologic significance of emotion in the production of abnormal mental states seems to be supported, however, by a study of this kind, and the fact that there is almost a constant increase in blood sugar values in emotional states that are organized into a picture of the psychoses seems to stand out clearly. Kooy has advanced the theory of the importance of the primitive emotional states in certain types of mental diseases. His conclusions in this regard appear to be amply substantiated by the results of the study herein recorded. The real value of his observation and of a wider study of blood sugar curves in pyschoses is apparent. It may mean eventually that the nondegenerative types of psychoses associated with depression will be viewed from a biologic point of view as a return to primitive emotional states in which the increase of glycogenic function serves the definite purpose of supplying increased muscular energy in carrying out maneuvers for the protection of the individual. In the static conditions represented by the inhibiting influence of emotionalism seen in depressed and anxious states, the glycogenic mechanism provides an increased ability to keep sugar in the blood preparatory to the expected muscular overaction in maneuvers of flight, concealment and other protective measures.

DISCUSSION

Dr. Smith Ely Jelliffe, New York: With regard to Dr. Schwab's statement that no precise diagnostic value is gained from these studies, I should like to ask him whether he would not use a different phrase, stating that there is no value for presently accepted diagnostic criteria. All observations are of value, and the only point of view is that the findings which he has narrated to us cannot yet be fitted into the imperfect schemes of diagnostic nosologic conceptions that we now have. There will come a time when our present unsatisfactory nosologic conceptions will be of great importance.

Dr. Walter Timme, New York: Dr. Schwab's conclusions are practically similar to those that most of us have obtained through a long and wide experience.

A sugar curve taken per se, without any other observations, has about as much value as the temperature alone, and the diagnosis of a patient's condition from it, the pulse rate or any single factor is impossible. In order to be of any value it must be taken in connection with many other conditions which the patient presents. Under such conditions one can possibly go a little further into the diagnostic values of the sugar curve. It perhaps bears the same relationship to the patient's condition that a metabolic study does, being valueless in diagnosing the patient's condition unless all the factors at the time of the experiment are taken into calculation.

To name one or two specific instances, a blood sugar curve must be interpreted in relationship to the point at which it begins, which is the original

blood sugar content. A patient whose sugar content is 0.09 and who has a rise in the sugar curve is entirely different from the patient who begins with a 0.06 sugar content and has a similar type of curve.

The so-called psychoneurotic patients and the army patients with neurocirculatory asthenia usually show a low sugar content as the first sign of disease. The slightest emotional disturbance will make the sugar content rise tremendously during the first and second hours and, depending on the character of the case and its compensations, it will go down.

Likewise the hebephrenic type of dementia praecox begins with a low sugar content, with a lower curve than the neurocirculatory asthenias, but with a fairly high sugar curve. The blood sugar curve must be taken in connection with other factors before a diagnosis can be determined.

DR. SCHWAB, in closing: In reply to Dr. Jelliffe's comments, my point is that at the present time we do not have sufficient differential diagnostic knowledge or information to make these things valuable.

All of the cases were studied with great care. I did not include clinical reports in this paper. All of the cases were examined in conjunction with the internal medical department of the hospital from every point of view, over quite a long period.

I excluded from the series all those instances in which the sugar curve might be influenced by other factors. This does not include any cases of cardiac disease, effort syndrome or diabetes. They were a group of neuropsychiatric cases studied primarily from the point of view of determining whether this procedure was valuable in a hospital study of the case. The initial hyperglycosemia was carefully considered in all of the cases, but it was of no value because of the variation which could not be interpreted. We have a curve as low as 0.04 in a person who had otherwise a perfectly normal case.

We found the highest blood sugar value in a young married woman, who had a fixed sensation of sweetness in her tongue and mucous membrane and was always haunted by a sensation of tasting sweet things. The initial first hour curve went up to 0.38, which was one of the highest initial curves, and the case was eliminated because of impossible differentiation from a diagnostic point of view.

MALIGNANT TUMORS OF THE NASOPHARYNX WITH INVOLVEMENT OF THE NERVOUS SYSTEM *

HENRY W. WOLTMAN, M.D.
Section on Neurology, Mayo Clinic
ROCHESTER, MINN.

The frequency and polymorphism of extranasopharyngeal symptoms seen in early cases of malignant disease of the nasopharynx does not seem to be widely appreciated. This applies particularly to the neurologic aspect. The absence, so far as I know, of any previous contribution covering this field and our experiences at the Mayo Clinic seem to justify a rather broad sketch of the neurologic phase of the subject.

New [1] has recently called attention to the relation of nasopharyngeal malignancy to other diagnoses, emphasizing the frequency of early extranasopharyngeal symptoms and the need of a wider understanding of the condition. His cooperation and skill enabled us to explain many unusual and difficult cases referred to the neurologic department for what often seemed to be disease primarily involving the nervous system.

An early diagnosis is not always easy. Table 1 shows that of the twenty-five cases comprising this series, only one was correctly diagnosed. These twenty-five cases were included in a series of seventy-nine cases of malignant tumors of the nasopharynx reported by New.[2]

Fifteen of the tumors were squamous-cell epithelioma, and six were lymphosarcoma (Table 2). The origin of these growths is usually in the fossa of Rosenmüller. While benign tumors occasionally involve the nervous system by penetrating the base of the skull, such tumors have not been included in this series.

Reports of forty-four cases were found in the literature, although the type of case was seldom indicated in the title of the paper. The sequence of events in the history, and the extranasopharyngeal and necropsy findings are briefly tabulated in Table 3. Unfortunately, the neurologic symptoms did not interest many of the writers, and such details are often slighted with some such remark as "brain mischief."

---

* Read before the Section on Nervous and Mental Diseases at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. New, G. B.: Relation of Nasopharyngeal Malignancy to Other Diagnosis, Minn. Med. **4**:419-422, 1921.

2. New, G. B.: Syndrome of Malignant Tumors of the Nasopharynx: A Report of Seventy-Nine Cases, J. A. M. A. **79**:10 (July 1) 1922.

TABLE 1.—Erroneous Diagnosis and Treatment in Twenty-Five Cases of Malignant Tumors of the Nasopharynx, with Involvement of the Nervous System

Diagnosis or Type of Treatment	Cases
Tonsillectomy	6
Extraction of teeth	6
Dissection of glands from the neck	6
Nasal sinuses drained	4
Trifacial neuralgia *	3
Nasal polyps and adenoids removed	4
Submucous resection	2
Operations on the nose	3†
Paracentesis of the tympanic membrane	2†
"Abscess" lanced in the throat	1†
Hodgkin's disease	1
Mumps	1
Pituitary tumor	1
Dementia paralytica	1
Syphilis	1
Nasopharyngeal sarcoma	1

* Alcohol injections and nerve sections.
† Several operations.

TABLE 2.—Involvement of the Cranial Nerves in Twenty-Five Cases of Malignant Tumors of the Nasopharynx *

Type of Tumor	Cases	Nerves Involved: First †	Second ‡	Third	Fourth	Fifth (Sensory)	Fifth (Motor)	Sixth	Seventh	Eighth §	Vago-Accessory: Palate¶	Vago-Accessory: Vocal Cords	Eleventh (Spinal)	Twelfth #
Squamous cell epithelioma	15	..	1	2	2	6	4	10	1	..	4	1	1	4
Adenosarcoma	1	..	1	..	..	1	..	..	..	..	..	..	..	..
Lymphosarcoma	6	..	1	..	..	3	1	6	..	..	2	2	2	1
Sarcoma	2	..	1	1	1	1	1	1	..	..	..	..	..	..
Mixed cell sarcoma	1	..	1	1	1	..	..	1	..	..	..	..	..	..
Total	25	?	5	4	4	11	6	18	1	?	6	3	3	5

* Males, 20; females, 5; age of patients with sarcoma, 6 to 68 years; average age, 49.3 years. Age of patients with epithelioma, 35 to 64 years, average 49.1 years. Onset of first symptoms in cases of carcinoma, six weeks; of sarcoma, four weeks; longest duration in cases of carcinoma, five years; of sarcoma, three years; average duration, 1.4 years and 1.2 years, respectively.

† The frequent nasal obstruction makes it impossible to determine involvement.

‡ Choked disks, bilateral once and unilateral twice. Secondary optic atrophy, homolateral once. Simple optic atrophy with homolateral blindness and heterolateral temporal hemianopia once.

§ Loss of hearing and tinnitus in at least one half of the cases, probably due to eustachian tube obstruction.

¶ Difficult to determine because of mechanical displacement or direct involvement of the muscle by the tumor.

In one case, hemiatrophy of the tongue was the first and only complaint.

TABLE 3.—Reported Cases of Tumor of the Nasopharynx Having Neurologic Complications

Author	Date	Sex and Age	Symptoms and Course	Clinical Findings (Extranasopharyngeal)	Diagnosis	Operative and Necropsy Findings
Ord, W. M.: Case of polypus nasi, extending upwards, and producing absorption of the body of the sphenoid bone, and obliteration of the internal carotid artery, followed by abscess of the brain, Brit. M. J., 1856, pp. 471-472	1858	M 50	Polyp removed thirty years before; deaf; blind in right eye; epilepsy; left hemiplegia	Deaf; blind in right eye; right internal strabismus; left hemiplegia	Polyp	Erosion of sphenoid; obliteration of internal carotid; three brain abscesses
Fleury: Polype fongueux (cancéreux) s'étendant à l'arrière-gorge, à la narine droite, pénétrant dans la cavité orbitaire, dans le sinus sphénoidal, et perforant la base du crâne après avoir détruit le corps du sphénoide, Bull. Soc. de chir. de Paris **4**: 447-449, 1864	1863	M 20	Pain in right side of face; nasal obstruction; right proptosis; erysipelas; died three months after onset	Right proptosis; pupil immobile; "eye lost"	Polyp fongereux (cancéreux)	Tumor eroding sphenoid and ethmoid; softening of adjacent brain
Verneuil, quoted by Veillon: Contribution à l'étude des tumeurs malignes naso-pharyngiennes, Paris, 1874	1867	M 40	Enlarged right cervical glands for three months; right proptosis and complete ophthalmoplegia; deafness; pain right side of head and nasal obstruction; death	Right proptosis; paralysis right third, fourth and sixth nerves, partial seventh and twelfth; deafness	Embryonic sarcoma	Erosion of the sphenoid with involvement of right second, third, fourth, fifth, sixth, seventh, eighth, tenth, left second, third, fourth and sixth nerves; dura intact
Verneuil and Schweich, quoted by Laval, F.: Destumeurs malignes du naso-pharynx, (Etude clinique), Toulouse, 1904; Arch. internat. de laryngol. **19**: 55-75, 1905	1867	F 40	Pain in left side of neck; deafness; death...	Left ptosis; mydriasis; facial palsy....	Sarcoma	
Verneuil and Flour, quoted by Laval.....	1873	F 39	Tumor of neck for seven years.....	Vocal cord paralyzed, due to gland....	Carcinoma?	
Veillon, F. T.: Contribution à l'étude des tumeurs malignes naso-pharyngiennes, Paris, 1874	1874	M 14	Swelling of left cheek; proptosis, nasal obstruction; hemorrhage; dysphagia; amaurosis on left; removal of tumor; erysipelas; nephritis; exitus one month after first seen	Left eye blind; left facial paralysis; left deafness	Sarcoma	Erosion of sella, of left sphenoid wing, left orbit with destruction and friability of second, third and sixth nerves and ocular muscles; erosion of left anterior fossa and right anterior fossa; extension along fallopian tube and injury of left facial nerve by pressure; metastasis to kidneys, mesentery, lungs, and spleen
Weinlechner: Verzweigtes Sarcom in der Nasen Rachen-augenhöhle mit Verdrängung des Bulbus; ungeheilt, Berl. d. k. k. Krankenanst, Rudolph-Stiftung in Wien 1876, p. 350	1876	M 14	Pain, nasal obstruction; right proptosis; blind	Loss of right vision; optic atrophy....	Sarcoma	
Bryk, quoted by Laval.....	1881	28	.....	"Fourth ventricle nuclei" involved.....	Round-cell sarcoma	
Shrady, G. F.: Removal of a large naso-pharyngeal tumor with extensive attachments to base of skull. Unexpected brain complications, death, Med. Rec., **22**: 311-314, 1882	1882	M 14	Occlusion of left nostril for four years; polyp removed; left exophthalmos; operation; death	No neurologic findings clinically (see necropsy findings)	Fibro-sarcoma	Tumor 2 cm. in diameter penetrating the foramen lacerum medium into the middle fossa
Weir, R. F.: Fibro-sarcoma of the nose, removed by Chassaignac's operation; recurrence in the brain, New York M. J. **45**: 282, 1887	1887	M 42	Obstruction of right nostril; hemorrhages....	Left blindness and divergent squint....	Fibro-sarcoma	Operation showed extension through the sphenoid and ethmoid

Fox, S. A.: Naso-pharyngeal carcinoma. Report of a case, with a consideration of the treatment of the disease, New York M. J. **51**: 259-260, 1890	1890	M 40	Bregmatic and frontal headaches for eleven months; nasal obstruction, deafness, diplopia	Strabismus; optic disks clouded; left hand weak	Epithelioma	Erosion of 3 inch opening through the middle fossa, involving the body and wing of the sphenoid; petrous temporal bone
Roncalli, F.: Sarcoma of naso-pharynx; fatal case, with necropsy, Rep. Superv. Surg.-Gen. Mar. Hosp. **19**: 151, 1890-1891	1890	M 40	Fullness and soreness of throat for two months; dysphagia	External and internal ophthalmoplegia	Sarcoma	Erosion of ethmoid and sphenoid
Ingals, E. F.: Fibro-sarcoma of naso-pharynx, Internat. Clin. **3**: 336-342, 1891	1891	M 39	Deaf for one year; pain in occiput; dysphagia; pushes food down throat with finger	"Diabetes insipidus;" urine specific-gravity 1.003, passes 16 to 18 pints each day; tongue paralyzed and atrophic	Fibro-sarcoma?	
Mülfarth, M. L.: Ueber maligne Geschwülste des Nasenrachenraumes, Köln, 1893	1893	F 26	Dysphonia; dysphagia	Paralysis of the right and left sixth nerves	Giant-cell sarcoma	
Roncalli, F.: Sarkom des Nasenrachenraumes, 1 Fall, Jahresb.u. d. chir. Abt. d. Spit. zu Basel (1892), 1894, p. 19	1894	M 43	Impaired hearing, left side, three months later right side also; left cervical glands; two years after nasal obstruction, proptosis, divergent squint and blindness; pneumonia; death three months later	Left cervical glands enlarged; proptosis; complete palsy third nerve; choked disk; blindness	Lympho-sarcoma	Erosion of the base and dura; metastasis to the gastric mucosa; gangrenous pneumonia; brown atrophy of the heart, spleen and liver
Alexander, quoted by Laval.....	1895	40	.....	Paralysis of the palate and sixth nerve	Sarcoma	
Etiévant, L.: Quelques considérations sur les phénomènes asphysiques provoqués par les polypes naso-pharyngiens; un cas de paresthésie du femorocutané externe accompagnant un lympho-sarcoma du pharynx, Rev. Internat. de rhinol., otol. et laryngol. **6**: 92, 1896	1896	M 18	Nasal obstruction for five months; pain under the left eye; two months later tracheotomy; anesthesia of the area supplied by the left femorocutaneous nerve	Anesthesia of the area supplied by the left femorocutaneous nerve; paralysis of the left third, fourth and sixth nerves	Lympho-sarcoma	
Hubbard, T.: The history and necropsy of a case of fibro-sarcoma of the naso-pharynx and middle cerebral fossa; associated conditions; ethmoiditis; empyema of the sphenoid cell; otitis media; pachymeningitis, Arch. Otol., **26**: 168-174, 1897	1897	M 50	Pain in left side of head for ten months; diplopia; loss of vision of left eye	Left eye, vision poor, pupil rigid; abducens palsy	Small round-cell fibrosarcoma	Erosion of the tumor through the left middle fossa from the sphenoid to the foramen ovale; pus in the sphenoid
Hellat, P. P.: Cancer of the nasopharynx, Vrach. **21**: 1019-1021, 1900	1900	43	Coryza for six months, nasal obstruction; deafness; death	Anesthesia of the pharynx; cord palsy; rapid pulse and respiration; hemiparesis of the tongue	Carcinoma	
Ratinow, quoted by Laval.....	1900	..	Palsy of the cranial nerves for two months; death	"Palsy of the cranial nerves".....	Carcinoma	
Jackson, C.: Primary carcinoma of the nasopharynx. A table of cases, J.A.M.A. **37**: 371-377 (Aug. 10) 1901	1901	F 23	Pain in right side of face and ear for one year; partial ankylosis of the jaw	Low grade optic neuritis; twitching of the right facial muscles	Columnar epithelioma	
Lotzbeck, quoted by Jackson.....	1901	F 37	.....	Bilateral proptosis and amaurosis.....	Carcinoma	
St. Mary's Hospital, quoted by Jackson...	1901	M 45	Left nasal obstruction for two and one-half years; headache; epistaxis; dysphagia; vertigo	Cervical glands; "left strabismus;" impairment of the right sensory fifth nerve and facial palsy	Epithelioma	
Compaired, quoted by Laval.....	1902	M 48	Pain for four months; nasal obstruction; loss of vision	Proptosis, blind in one eye; ophthalmoplegia	Epithelioma	
Bronner, quoted by Laval.....	1903	63	"Cerebral symptoms" for eight months.....	Proptosis; optic atrophy.....	Carcinoma	

TABLE 3.—Reported Cases of Tumor of the Nasopharynx Having Neurologic Complications—(*Continued*)

Author	Date	Sex and Age	Symptoms and Course	Clinical Findings (Extranasopharyngeal)	Diagnosis	Operative and Necropsy Findings
Stenger: Maligner Tumor des Nasenrachenraumes: eitrige Mastoiditis, Arch. f. Ohrenh. **61**: 247-250, 1904	1904	M 54	Pain in the right side of head and face for sixteen months; tinnitus; diplopia for six months; ptosis; loss of vision; two weeks later sudden tetraplegia and death	Hyperemic disk, external ophthalmoplegia; hyperesthesia and hyperalgesia of right side of face; impaired hearing on the right side	Sarcoma; mastoiditis	
Baldwin, Kate W.: Malignant growth of the nasopharynx: A report of two cases, J. Ophth. and Oto-Laryngol., **2**: 12-17 1908	1908	F 42	1904, left earache and discharge; 1905, pain in right side of face and head; loss of memory, irritability, epistaxis; 1906, right ophthalmoplegia; 1907, nasopharyngeal tumor found; right eye blind	Deafness on right side; paralysis of right second, third and fourth nerves, and sensory part of fifth nerve after July, 1906	Epithelioma	
Brown, C. M.: Carcinoma of the nasopharynx, Laryngoscope **21**: 1069, 1911	1911	M 49	Pain in the left temple for six months; discharge from the left nostril and ear; left side of face numb; diplopia; and ptosis eight months later	"Diplopia"; ptosis; impaired sensation (subjective?) of the left side of the face	Squamous cell carcinoma	Died of meningitis; the neurologic signs were all shortly antimortem in their appearance
Guthrie, T.: Carcinoma of the nasopharynx in a girl aged 17, J. Laryngol. **26**: 449-452, 1911	1911	F 17	Nasal obstruction; pain in left side of face and ear; epistaxis, syncopal attacks; deafness; cervical glands enlarged; three months later left proptosis and blindness; dysphagia	Left cervical glands enlarged; impaired hearing; proptosis, blindness	Carcinoma	
Aboulker, H. (Garel): Contribution à l'étude des tumeurs malignes du naso-pharynx, Bull. d'oto-rhino-laryngol. **15**: 115-134, 1912	1912	M 45	Nasal obstruction for six months; headache; death eight months later	"Evidence of compression of nerves at base of skull"	Epithelioma	
Todd, H.: Malignant disease of left sphenoidal region; proptosis with blindness of eye on same side; enlarged cervical glands on both sides, Proc. Roy. Soc. Med., Laryngol. Sect. **6**: 19, 1913	1912	M 52	.....	Left proptosis and optic atrophy.....	Epithelioma?	
Courtillet and Aboulker; quoted by Aboulker	1912	M 42	Headache on the right side for seventeen months; right nasal obstruction; deafness and blindness; strabismus; death eleven months later	Right deafness and blindness; strabismus; vocal cord palsy	Fibrosarcoma	
Molinié, J.: Cancer du naso-pharynx, Larynx, l'orielle et le nez **6**: 75-78, 1913	1913	M 40	Pain in the right side of neck for four months; deafness; cervical glands enlarged; diplopia; nasal obstruction; dysphagia; death	Right cervical glands enlarged; deafness; "diplopia"	Cancer	
Oppikofer, E.: Ueber die primären malignen Geschwülste des Nasenrachenraumes, Arch. f. Laryngol. u. Rhinol. **27**: 526-564, 1913	1913	M 61	Pain in right half of head, ear and tongue for six months	Proptosis; paralysis of the right third, fourth, sixth, tenth and twelfth nerves	Carcinoma	
		M 19	Nasal obstruction for one and one-half years; dysphagia; deafness and headache for four months	Right vocal cord palsy, and deviation of the tongue to the right	Large-cell sarcoma	
		F 58	Impaired hearing for three months, after nine and one-half months of bulbar symptoms	Paralysis of the right side of palate and entire tongue	.....	Erosion through the sphenoid and petrous temporal bone, not penetrating the dura, but touching it; involvement of the right fourth, fifth and sixth nerves, and left twelfth nerve
		M 17	Impaired hearing for five months, pain in the right jaw and occiput for two months; right facial palsy eight months after onset; ophthalmoplegia; death	Right pupil small; paralysis of the right superior rectus, external rectus and right facial nerve; deaf	Endothelioma	Metastasis to cervical glands; base of brain pushed upward near the sella; third, fourth, fifth and sixth nerves involved intracranially, seventh nerve extracranially (gland); gasserian ganglion invaded

Oppikofer, E. (Continued)		F 13	Headache for two months; dysphagia.....	Bilateral external rectus palsy and right half of tongue	Carcinoma	Tumor attached to vertebral column, extending downward to the hyoid, upward through the sphenoid; dura not penetrated
		M 54	Epistaxis for seven months; impaired mastication for five months; ophthalmoplegia eight months after onset; death nine months later	Palsy of the right palate and third, fourth and sixth nerves	Lymphosarcoma	
		M 30	Difficulty in breathing for one month; pain in the right ear and occiput; hoarseness and diplopia	Involvement of the ninth, tenth, eleventh and twelfth nerves on the left and both sixth nerves	Sarcoma	Dura elevated from base of skull near the petrous part of the temporal bone
Finzi, A.: Fall von Tumor des Nasenrachenraumes mit Metastasen an der Gehirnbasis und im Rückemark, Mitt. d. Gesellsch. f. inn Med. u. Kinderh. in Wien **13**: 161-163, 1914	1914	M 22	Pus and blood from the cervical gland for two years; pain on left side of face and head for one year; left nasal obstruction; deafness	Bilateral cervical glands; anosmia on left; left deafness; proptosis; complete left third and sixth, and fifth motor and sensory nerve palsies; palate weak on left side; hyperesthesia over the fifth and sixth dorsal segments; sixth and seventh dorsal spines tender, right positive Babinski sign	Sarcoma ?	
Oppikofer, E.: Primäres Lymphosarkom des Nasenrachens, Cor.-Bl. f. schweiz. Aertze **46**: 1177, 1916	1916	M 17	Pain in the region of the right side of face	Right proptosis and external ophthalmoplegia	Endothelioma	Dura elevated, but not penetrated
Stähli, J.: Ueber augenmuskellähmung als initialis Symptom von Malignem Nasenrachentumor, Klin. Monatsbl. f. Augenh. **65**: 888-891, 1920	1920	F 62	Left abducens palsy for four and one-half months; improvement for three months; returned nine months after onset; nasal obstruction eleven months after onset; ptosis and amaurosis on the left	Impaired vision on the left; right ptosis; dilated pupils; fundi normal; bilateral abducens palsy	Carcinoma	
		M 49	Slight headache for one month; paralysis of the right third nerve; blind in the right eye	Right blindness and third nerve palsy	Sarcoma	

SYMPTOMS

The clinical picture at first suggests a melange of head symptoms and signs, but on closer inspection a more precise formulation becomes possible. Occasionally it is difficult to decide whether the involvement of the nervous system was caused by the tumor, or by later complication; for example, in Sédillot's [3] case a cerebral infection apparently followed operation; in Ord's [4] case three brain abscesses were found at necropsy; in Brown's [5] case, the neurologic findings appeared shortly before death, and necropsy revealed basilar meningitis.

It is noteworthy that in sixteen of my twenty-five cases there were no nasopharyngeal symptoms. Pain in the face, side of the head, or ear was perhaps the commonest symptom, having been the chief complaint in fourteen of the cases; in five cases, however, it was altogether lacking. This group has been referred to in the literature as the neuralgic type. There was generalized headache in four cases. Paresthesia of the face without pain was an annoying complaint in five. Deafness and tinnitus in one or both ears are common, owing nearly always to obstruction of the eustachian tube by the growth. Seven patients complained of diplopia and three of blindness, ptosis, or exophthalmos. Stähli,[6] in two well reported cases, shows that ocular palsies may be transitory and for a long time the only symptom of nasopharyngeal tumors.

In the nasopharyngolaryngeal group, six patients complained chiefly of nasal obstruction, two of dysphagia, and two of recurrent aphonia, due to vocal cord palsy. In a miscellaneous group, five patients had cervical glandular enlargement, two had syncopal and epileptiform attacks, one had a psychosis (Case 22), and one had pain in the leg due to metastasis in the spine with radiculitis (Case 9).

RESULTS OF EXAMINATION

The nasopharyngeal findings will be omitted, since they have been taken up in detail by other writers on the subject. For the incidence of involvement of the various cranial nerves and certain comments on these, the reader is referred to Table 2.

The abducens was the nerve most often affected (eighteen of the twenty-five cases), the third and fourth less often. There was objec-

3. Sédillot: Polype nasal; racines pénétrant dans le sinus sphénoïdal, Soc. de méd. de Strasb. (1858-1863) **1**:190-192, 1864.

4. Ord, W. M.: Case of Polypus Nasi, Extending Upward, and Producing Absorption of the Body of the Sphenoid Bone, and Obliteration of the Internal Carotid Artery, Followed by Abscess of the Brain, Brit. M. J., 1858, pp. 471-472.

5. Brown, C. M.: Carcinoma of the Naso-Pharynx, Laryngoscope **21**: 1069, 1911.

6. Stähli, J.: Ueber Augenmuskellähmung als initialis Symptom von malignem Nasenrachentumor, Klin. Monatsbl. f. Augenh. **65**:888-891, 1920.

tive sensory disturbance in the domain of the fifth nerve in eleven cases, the motor branch being involved in six. The dissociations were often peculiar. In Case 10 there was complete loss of pain sensibility, partial loss of temperature sensibility, and slight impairment of tactile sensibility over the left half of the face. The motor root was almost completely paralyzed. It is the peripheral portion of the nerves that is most often caught in the tumor growths but the gasserian ganglion has been known to be involved (Oppikofer).[7] I found no necropsy reports of involvement of the fifth nerve within the central nervous system, so that the peculiar dissociation and distribution of the anesthesia cannot be explained on this basis. Trigeminal involvement was mentioned only five times in the cases collected from the literature.[8] In one (Finzi's),[9] there was motor involvement also. Doubtless this low incidence is apparent rather than real, since most of the cases were reported solely from the rhinologic standpoint. In none was curious dissociation and distribution of the anesthesia emphasized.

The facial nerve was not paralyzed in any of our cases; only one patient, Case 12, showed fibrillary tremors in the facial muscles. In five of the forty-four cases from the literature the facial nerve was involved: four times in combination with ocular palsies and one with fifth nerve palsy. The vestibular nerve is usually intact. Oppikofer [7] says that the vestibular reactions were normal in all of his cases. The ninth, tenth, and eleventh nerves are said to be paralyzed by glandular involvement rather than by the primary growth. That this is always true is doubtful. These nerves might easily be involved by the growth near the jugular foramen. Palatal immobility may be caused by direct pressure from the tumor and by involvement of the levator palati muscle (Trotter),[10] as well as by nerve injury. The twelfth nerve is commonly affected, and generally extracranially near its exit through the anterior condyloid foramen.

---

7. Oppikofer, E.: Ueber die primären malignen Geschwülste des Nasenrachenraumes, Arch. f. Laryngol. u. Rhinol. **27**:526-564, 1913.

8. St. Mary's Hospital quoted by Jackson, C.: Primary Carcinoma of the Nasophyarynx: A Table of Cases, J. A. M. A. **37**:371-377, 1901 Stenger: Maligner Tumor des Nasenrachenraumes: eitrige Mastoiditis, Arch. f. Ohrenh. **61**:247-250, 1904. Baldwin, Kate W.: Malignant Growths of the Nasopharynx: A Report of Two Cases, J. Ophth. & Oto-Laryngol. **2**:12-17, 1908. Brown, C. M.: Carcinoma of the Naso-Pharynx, Laryngoscope **21**:1069, 1911. Guthrie, T.: Carcinoma of the Nasopharynx in a Girl Aged Seventeen, J. Laryngol. **26**:449-452, 1911.

9. Finzi, A.: Ein Fall von Tumor des Nasen-Rachenraumes mit Metastasen an der Gehirn-basis und im Rückenmark, Mitt. d. Gesellsch, f. inn. Med. u Kinderh. in Wien. **13**:161-163, 1914.

10. Trotter, W.: On Certain Clinically Obscure Malignant Tumors of the Nasopharyngeal Wall, Brit. M. J. **2**:1057-1059, 1911.

As a rule, several cranial nerves are affected simultaneously, particularly those entering the orbital cavity. Next in frequency is a combination of these with the trigeminal (six cases in the series). Solitary fifth nerve involvement and the jugular foramen group are next in frequency (three of each in the series). All combinations of cranial nerve palsy seem possible.

PATHOLOGIC REPORTS

Pathologic reports are rather scant (Table 3). As most of the growths arise near the orifice of the eustachian tube, it is readily seen why the cranial nerves are so extensively involved. The bony structures surrounding this area are for the most part made up of thin lamellae readily eroded; there are numerous foramina and fissures through which the growths may extend. The only heavy bones are the pars basillaris, the proximal portions of the sphenoid wings, and the petrous portion of the temporal bones. The sphenoid and the ethmoid are usually eroded early. The sphenomaxillary fissure, the orbital fissure and internal and inferior orbital plates and the foramen lacerum are readily penetrated. In several cases there was erosion of the tip of the temporal bone.

That direct involvement of the ocular muscles may occur is well shown by Veillon's [11] case. Involvement of the cranial nerves is for the most part extracranial. Even when the dura has been reached it may be elevated, but is rarely penetrated. Veillon has shown that bilateral chocked disk is not conclusive evidence of intracranial involvement, since in these cases it is usually caused by invasion of the orbital cavities.

Invasion of the pituitary region once led me to a wrong conclusion. The findings were typical of pituitary tumor (Case 1). Since this experience I have never neglected to examine the nasopharynx in cases of suspected pituitary tumor. Segui [12] says Jaboulay reported a case in which a nasopharyngeal tumor occupied the pituitary fossa, but he gives no bibliographic reference.

Metastasis is not common. In one of our cases (Case 9) there was metastasis to the lumbar spine, producing caudal symptoms. Enlarged glands in the neck in this case directed suspicion toward the nasopharynx; on examination a lymphosarcoma was found. Metastasis

---

11. Veillon, F. T.: Contribution à l'étude des tumeurs malignes nasopharyngiennes, Paris, 1874.

12. Segui, H.: Contribucion al estudio de los sarcomas de la nasofaringe; frecuencia y puntos de insercion, Rev. de med. y cirug. de la Habana **23**:241-248, 1918.

to the stomach (Roncalli),[13] mesenteries, lungs, kidneys, spleen (Veillon),[11] pleura and lungs (Benda,[14] Oppikofer) has been described.

SUMMARY

1. Malignant tumors of the nasopharynx are more common than is generally believed.

2. Early diagnosis is difficult because of the common incidence of early extranasopharyngeal symptoms; in sixteen of twenty-five cases there were no nasopharyngeal symptoms. Among early complaints and signs are pain in the face or side of the head, headache, deafness, tinnitus, diplopia, blindness, proptosis, paresthesia of the face, cervical adenopathy, dysphagia, aphonia, hoarseness, and malignancy in distant parts of the body.

3. Twenty-five cases with involvement of the nervous system were selected from seventy-nine cases of malignant tumor of the nasopharynx seen at the Mayo Clinic. Cranial nerves were usually involved extracranially, those passing through the orbital fissures most commonly, particularly the sixth. Next most often involved was the trigeminal; eleven of the twenty-five patients showed sensory changes and six motor paralysis.

4. In all unexplained cases of cranial nerve palsy, in suspected tumors of the gasserian ganglion, in paralysis of groups of cranial nerves constituting the various classical syndromes, such as the jugular foramen syndrome, in glandular enlargement of the neck, in metastatic malignant disease in which no primary growth can be discovered, and in all cases of suspected pituitary tumor, the nasopharynx should be adequately examined.

REPORT OF CASES

Case 1.—Mr. F. A. A., aged 33, came to the Clinic, Feb. 11, 1917, complaining of blindness of the right eye, stiffness of the neck, and headache. Three years before, he had had headache, vertigo, and blindness of the right eye, for six months; then he had been well until three weeks before, when he fainted and was unconscious for an hour; his neck became stiff and painful. He vomited and had slight headache. After removal of spinal fluid the headache stopped. A diagnosis of brain tumor had been made.

Examination of the nasopharynx was not made in this case. Vision in the right eye was 0 with atrophy of the nerve; in the left eye 6/7, with pallor of the nerve head on the temporal side and temporal hemianopia. Hearing was diminished on the left. A roentgenogram of the head showed destruction of the sella turcica. A pituitary tumor was suspected.

At operation, a tumor 2 cm. in diameter, under and to the right of the optic nerve, was removed. The patient died several days later. At necropsy

13. Roncalli, F.: Sarkom des Nasenrachenraumes, 1 Fall, Jahresb. u. d. chir. Abt. d. Spit. zu Basel (1892), 1894, p. 19.

14. Benda: Quoted by Oppikofer, Footnote 7.

an irregular extradural, degenerating sarcoma 5.5 by 4.5 by 3 cm. was found. It completely filled the eroded area of the ethmoid and sphenoid bones and had eroded the petrous portion of both temporal bones.

This case was of interest because clinically it resembled pituitary tumor. Unfortunately, the tumor removed at operation was lost before sections were made. It seemed to be completely encapsulated and differed in appearance from the mass extending upward from below; however, we must assume that the tumor was part of a mass extending upward from the nasopharynx.

Case 2.—Mrs. F. E. N., aged 36, came to the Clinic, Sept. 23, 1918, complaining of ptosis of the right eyelid and impaired vision of one year and ten months' duration. She had had headache, numbness of the right side of the face, and deafness on the right for one month.

An adenocarcinoma of the posterior pharynx was found. On the right were central scotoma, optic atrophy, ptosis, and a small pupil which did not dilate on instillation of cocain, presumably a sympathetic paralysis. Vision in the left eye was normal. The patient died Feb. 11, 1919.

Case 3.—Mr. O. M. F., aged 54, came to the Clinic, Sept. 17, 1918, complaining of pain in the region of the nose and forehead on the right side, of one and one-half years' duration, and diplopia for five months. Several operations had been performed for removal of nasal polyps. An epithelioma of the right nasopharynx and slight enlargement of the left cervical glands were found. The right external rectus was paralyzed. The patient died, Nov. 16, 1919.

Case 4.—Mr. M., aged 45, came to the Clinic, May 15, 1919, because of sore throat lasting one and one-half months. The throat had been lanced several times but no pus found. He had had a hemorrhage from the nose, and for one week he had been strangled when swallowing.

An epithelioma, filling the right nasopharynx and extending to the hypopharynx, and enlarged right cervical glands were found. The right eyelid drooped slightly and the right pupil reacted slowly to light and was smaller than the left, probably due to sympathetic paralysis, Horner's syndrome. There were moderate dysphagia, definite weakness of the right sternocleidomastoid and trapezius muscles, and paralysis of the right vocal cord.

Case 5.—B. N., a girl, aged 6 years, was brought to the Clinic, July 9, 1919, because of nasal discharge and an ache in the left side of the head of five weeks' duration. One month before, the left eye had turned in. Adenoids had been removed without relief of symptoms.

A sarcoma filling the nasopharynx was found. A roentgenogram of the head showed a cloudy antrum and destruction of the sella turcica. External and internal ophthalmoplegia on the left was complete.

Case 6.—Mr. A. C., aged 49, came to the Clinic, Jan. 17, 1920, because of catarrh of many years' duration. For three months the patient had noticed a mass on the right side of the neck, drooping of the right lid, diplopia and tingling, and a "shaving" pain in the region of the right temple and face.

An ulcerated area was found in the right nasopharynx which on biopsy proved to be squamous-cell epithelioma. Cervical glands of each side were enlarged. There was slight exophthalmos on the right, and the external rectus muscle was paralyzed.

Case 7.—Mr. W. A. S., aged 44, came to the Clinic, Jan. 27, 1920, because of pain and swelling in the neck of one and one-half years' duration. For one year the right ear had ached and hearing had diminished; for five months

hoarseness and regurgitation of fluid through the nose had been noticeable, and for one month the right side of the tongue had felt stiff.

A lymphosarcoma filling the nasopharynx and enlarged submaxillary glands on each side were found. The patient could not hear a watch tick on the right, and the right half of the tongue was paralyzed and atrophied. Reexamination, July 1, showed, in addition, paralysis of the right half of the soft palate, and of the right vocal cord and moderate weakness of the right sternocleidomastoid and trapezius muscles. The patient died, April 2, 1921.

Case 8.—Mr. E. F. B., aged 64, came to the Clinic, Feb. 9, 1920, complaining of pain in the right ear and face of three years' duration.

An extensive squamous-cell epithelioma (biopsy) was found filling the right nasopharynx and obstructing the orifice of the eustachian tube. The right cervical glands were enlarged, and the right temporal region bulged diffusely; the right eyelids were sewn shut. Other positive findings were complete sensory and motor paralysis of the right fifth nerve, and inability to hear a watch tick on the right.

Case 9.—Mr. F. D., aged 60, came to the Clinic, May 15, 1920, because of pain in the left sacro-iliac area of eight months' duration. A gland in the left cervical region had been enlarged for two years.

A slight bulge in the left nasopharynx, 0.5 cm. in diameter, on biopsy proved to be a lymphosarcoma. The cervical glands on each side were enlarged. A roentgenogram of the chest was negative. Other neurologic findings were absence of knee and Achilles' reflexes, and loss of touch, pain and temperature sensibilities over the distribution of the left fourth and fifth lumbar segments. A roentgenogram showed a lesion of the fourth and fifth lumbar vertebrae. The pain in the back and leg and the clinical picture were typical of tumor of the cauda equina. A diagnosis was made of malignant growth in the lumbar spine, metastatic from the lymphosarcoma found in the nasopharynx. The patient died, Oct. 13, 1921.

Case 10.—Mr. H. A. C., aged 30, came to the Clinic, June 26, 1920, complaining of fullness, pain and loss of hearing in the left ear of two years' duration, for which submucous resection, tonsillectomy, extraction of teeth, sinus operation, and four or five paracenteses had been performed. For four months there had been numbness of the left side of the face and recently severe general headache and vertigo.

A lymphosarcoma, verified by biopsy, was found filling the left upper pharynx and blocking the orifice of the eustachian tube. There was slight fullness of the left parotid region; the cervical glands on either side were enlarged. Other findings were left exophthalmos with choked disk and absence of the corneal reflex, almost complete paralysis of the left external rectus, paralysis of the left motor fifth nerve, loss of pain sensibility, moderate impairment of temperature sensibility, and slight diminution of tactile sensibility over the left half of the face and tongue.

Case 11.—Mrs. J. B., aged 56, came to the Clinic, Sept. 2, 1920, because of nasal obstruction of three months' duration. There had been pain over the right lip and nose and diplopia for two months. Operation had been performed on the nose, and the teeth had been extracted without relief.

A large lymphosarcoma (biopsy) obstructing the right nasopharynx and enlarged right cervical glands were found. The right external rectus muscle was paralyzed.

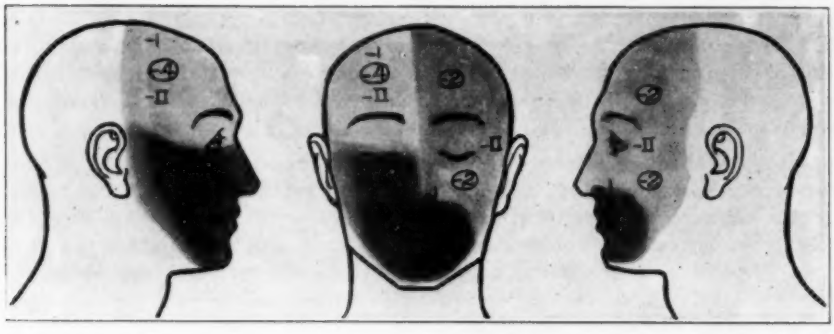

Fig. 1 (Case 12).—Oct. 16, 1920. Besides the sensory disturbance, the patient had a right choked disk, left papilledema, horizontal nystagmus to the left, rotary toward the right, complete bilateral paralysis of the sixth nerve; fibrillary tremors, but no weakness of the muscles supplied by the right motor fifth nerve; dysphagia; right patellar and Achilles reflexes more active than the left, and strongly positive Oppenheim, Rossolimo and Gordon reflexes on the left. Circled Arabic figures refer to loss of pain sensibility; Arabic figures to loss of tactile sensibility, and Roman figures to loss of temperature sensibility, on a basis of —1 to —4.

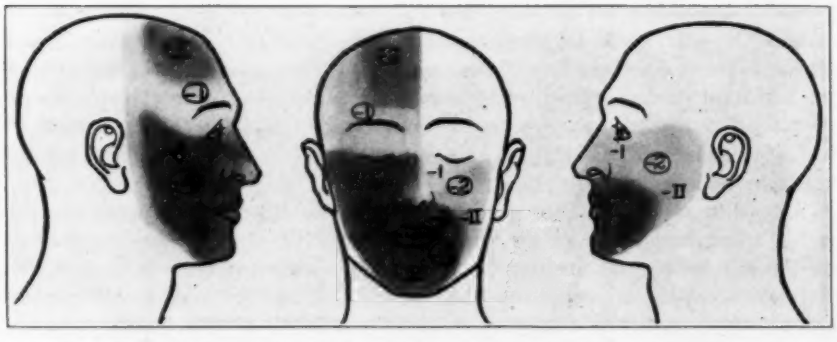

Fig. 2 (Case 12).—Feb. 9, 1921. Besides the sensory disturbance the patient had slight ptosis, horizontal nystagmus, complete paralysis of the sixth and motor fifth nerves, and moderate hemiparesis and hemiatrophy of the tongue on the right side. The right patellar reflex was slightly more active than the left, and the Babinski sign was questionable. The Oppenheim, Gordon, and Rossolimo reflexes were strongly positive on the left.

CASE 12.—Mr. T. F., aged 49, came to the Clinic, Oct. 14, 1920. For five years he had had a heavy feeling in the region of the right ear. Two years before, a gland in the right cervical area had enlarged; for one year there had been diplopia, for six months the right half of the face had been numb and burned, and for five months he had had a sensation of strangling.

A squamous-cell epithelioma (biopsy) obstructing the orifice of the right eustachian tube was found. Successive neurologic findings are indicated in Figures 1, 2, and 3.

CASE 13.—Mr. W. A., aged 63, came to the Clinic, Dec. 8, 1920, because of nasal obstruction of one and one-half years' duration. Deafness of the left ear for six months and numbness of the left side of the face and diplopia for one month were accompanying symptoms. Twice a mass had been removed from the patient's nose, and excision of cervical glands, tonsillectomy, and extraction of teeth had been performed without relief.

A lymphosarcoma (biopsy) obstructing the left nasopharynx and enlarged cervical glands on both sides were found. The external recti were paralyzed.

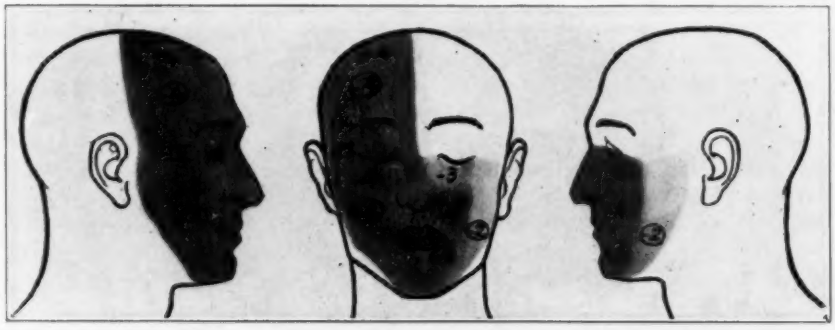

Fig. 3 (Case 12).—Aug. 11, 1921. Besides the sensory disturbance, the patient had complete external and internal ophthalmoplegia, paralysis of the motor fifth nerve, and hemiparesis, hemiatrophy, and fibrillary tremors of the tongue on the right side.

CASE 14.—Mr. H. G. D., aged 62, came to the Clinic, Dec. 22, 1920, complaining of obstruction of the left nostril and pain in the left side of the head of four months' duration and of diplopia for two months.

A highly malignant, squamous-cell epithelioma (biopsy) was found filling the left nasopharynx. The left external rectus muscle was palsied. The patient died, May 17, 1921.

CASE 15.—Mrs. C. L., aged 58, came to the Clinic, Jan. 26, 1921, complaining of an enlarged cervical gland of ten months' duration and of diplopia for four months.

A highly malignant squamous-cell epithelioma (biopsy) was found occupying the posterior wall of the pharynx. The cervical glands on each side were enlarged. There were deafness and diplopia.

CASE 16.—Mrs. F. C. B., aged 54, came to the Clinic, Feb. 5, 1921, because of blindness of the right eye. The trouble had begun three months before with pain in the right temple and tinnitus and diminished hearing in the right ear. For two months the patient had had right nasal obstruction, difficulty

in opening the mouth, numbness, sharp sticking pain, and swelling over the right side of the face, and right temple. One month before, the right eyelid had drooped. Two weeks before, the right eye had begun to protrude, became immobile, and blind.

A nasopharyngeal tumor on the right side of the nasopharynx was found blocking the orifice of the eustachian tube and extending past the middle line. The right submaxillary gland was enlarged; the antrums were cloudy on transillumination. The neurologic findings are shown in Figure 4.

Case 17.—Mr. H. C. C., aged 47, came to the Clinic, Feb. 7, 1921, complaining of "mumps" on the left side, persisting for two years. For eight months he had had tinnitus and deafness of the left ear; for four months, slight aching of the left ear and numbness of the left cheek and mouth, and for two weeks, transitory diplopia.

A slightly malignant, squamous-cell epithelioma (biopsy) in the vault, with obstruction of the orifice of the eustachian tube on the left, was found. There was anesthesia of the left side of the face and tongue. Subjectively a numb, crawling sensation was felt on the left side of the face, and there was slight diplopia.

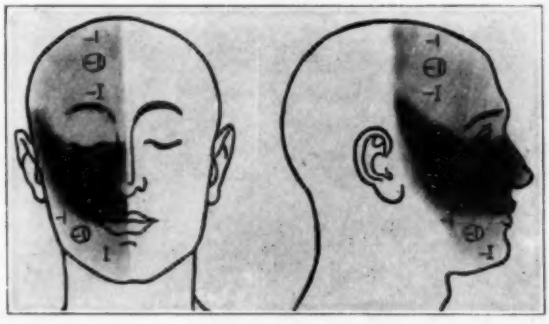

Fig. 4 (Case 16).—Besides the sensory disturbances the patient had anosmia on the right; blindness, blurred disk, proptosis 4 mm., complete external and moderate internal ophthalmoplegia on the right; paralysis of the right motor and fifth nerves; deafness in the right middle ear; paralysis of the right half of the palate, and slight hemiparesis of the tongue on the right.

Case 18.—Mr. J. E. R., aged 51, came to the Clinic, Feb. 22, 1921, complaining of a "squeezing" pain in the right temple and over the right eye of one year and two months' duration. He had had diplopia for five months. A nasal polyp had been removed, several alcohol injections given, the antrum irrigated, and the teeth extracted without relief.

An ulcerating epithelioma (biopsy) was found occupying the fossa of Rosenmüller and obstructing the orifice of the eustachian tube. There was slight ptosis of the right eyelid; the left external rectus was paralyzed, and the left pupil was small. There was slight weakness and loss of pain sensibility of the right fifth nerve.

Case 19.—Mrs. C. W. I., aged 57, came to the Clinic, April 20, 1921, complaining of catarrh and hemorrhages from the nose of three years' duration. For one year, she had had pain in the head, nasal obstruction with loss of the sense of smell, earache, tinnitus, and deafness on both sides, and for three months, diplopia.

An extensive, highly malignant, squamous-cell epithelioma (biopsy) obstructing the orifices of both eustachian tubes was found in the nasopharynx. The right external rectus was completely paralyzed; fibrillary tremors on both sides of the tongue were more marked on the left; atrophy of the left half of the tongue was advanced.

CASE 20.—Mr. F. W., aged 46, came to the Clinic, Aug. 4, 1921, complaining of enlarged glands of the neck and nasal obstruction on the left of one year's duration. Septic tonsils had been removed. For eight months, there had been a hissing noise with impairment of hearing on the left, and for three months, pain on the left side of the head and diplopia. Tonsillectomy and block resection of the glands in the neck had been performed; the antrum had been drained, teeth extracted, nasal polyps removed, and treatment for syphilis given without relief.

A tumor, probably an epithelioma, was found filling the left half of the nasopharynx. Cervical glands were enlarged on each side. The left external rectus was weak, hearing was diminished, and the left half of the palate was partly paralyzed.

CASE 21.—Mr. M. B., aged 35, came to the Clinic, Sept. 20, 1921, because of headache and diplopia of two months' duration. Nasopharyngeal symptoms were absent.

In the vault of the nasopharynx a highly malignant, squamous-cell epithelioma was discovered. The left external rectus was paretic, and the sella turcica and the sphenoid body were totally destroyed.

CASE 22.—Mr. C. W. S., aged 46, came to the Clinic, Dec. 9, 1921, complaining of drowsiness and loss of mental power. One brother and two sisters had migraine. The first symptom had been noticed two and one-half years before when the patient's disposition had begun to change. He had always been jolly and good natured, but he became irritable and vindictive; he flew into a rage because of children, and he was sour and morose. He had lost his business acumen and had been swindled out of $1,000. Continuously for two years he had had left frontal and occipital headaches, pounding in character. Diplopia had been an accompanying complaint. In October, 1919, a mass about 3 cm. in diameter had been excised from the left cervical region. In May, 1920, nasal polyps had been removed. Although blood tests were negative, he had been treated for general paresis. In November, 1920, the left antrum had been drained and teeth extracted. The patient soon began to have night terrors; he cried a great deal, he thought he was being fed fire and that he was drowning; he threatened to take his wife's life. He had lost all personal pride; he would spit or defecate anywhere. Intense pain and a pounding noise had been present in the left ear for one year. In April or May, 1921, tissue was excised from the nose for diagnosis and pronounced sarcoma. Three months before, attacks of syncope had come on, and two months before the left side of the face, the left arm, and leg had become "dead" and cold. Vision in the left eye had been poor.

A squamous-cell epithelioma (biopsy) of the left nasopharynx involving the eustachian tube was found. External swelling was noticeable in the left temporal region. The left cervical glands were enlarged. The patient was stupid, noncooperative and hoarse. His right antrum was cloudy on roentgen-ray examination. Vision in the left eye was poor. The pupil did not react to light either direct or crossed and was very small. The fundi were normal. Tactile sensibility was definitely impaired throughout the left side of the face,

and there was pain over the second and third divisions. The right motor fifth nerve was paralyzed. The patient did not seem to hear a watch on either side. Dysphagia was present; the vocal cord was fixed. Anesthesia of the pharynx and hypopharynx was present on the left, and there was incoordination in the finger to nose test on the left. The gait was ataxic. The Babinski and Chaddock reflexes were questionable on the left.

Case 23.—Mr. I. G., aged 36, came to the Clinic, Feb. 11, 1922, because of headache and transitory aphonia of eight or nine months' duration. For three years he had noticed enlargement of the left cervical glands, which had been removed in 1919 and in 1921. There had been dysphagia for four months, strabismus for three months, and syncopal attacks for two months.

A mass was found pushing the palate forward and filling the nasopharynx. Hearing was impaired and the palate palsied; the sixth nerve, vocal cord, sternocleidomastoid, and trapezius muscles, and tongue were paralyzed on the left.

Case 24.—Mr. M. L., aged 24, came to the Clinic, April 6, 1922, complaining of pain in the right eye, forehead, and maxilla of one year and three months' duration. Seven months before he had had an operation "to get the nerve," on the assumption that trifacial neuralgia was present. Roaring noise and impaired hearing on the right side had followed. Four months before, a similar operation had been performed. The patient had had diplopia for three months. He had been taking powders containing acetanilid, caffein, sodium bicarbonate, and charcoal for relief of pain for seven months and had noticed that during the past three or four weeks his face was becoming a dusky blue.

Examination revealed a tumor in the right nasopharynx, weakness of the right external rectus and complete sensory and motor paralysis of the right fifth nerve, and partial paralysis of the right seventh nerve, probably due to operation. The Bárány test was negative. Spectroscopic examination of the blood showed methemoglobin.

Case 25.—Mr. F. B., aged 33, came to the Clinic, May 5, 1922, because of constant dull pain over the left side of the face, frontal and temporal areas, of three and one-half months' duration. Five months before the left nostril had become obstructed and an operation had been performed. For four months earache had been severe on the left. Three and one-half months before, another operation on the nose had been performed without relief. For one and one-half months the patient had noticed enlarged left cervical glands which had been excised two weeks later, and impaired vision on the left. Two weeks before, swallowing had caused pain.

The soft palate was found to bulge because of a nasopharyngeal tumor, which biopsy proved to be mixed-cell sarcoma. Other findings were blindness, chocked disk of 3 diopters, loss of reaction to light, ptosis, limited rotation of the eye upward and downward, and paralysis of the external rectus muscle.

DISCUSSION

Dr. Gordon B. New, Rochester, Minn.: During the last six years, I have examined seventy-nine patients with nasopharyngeal tumors. Dr. Woltman has reported on the neurologic findings in twenty-five of these cases. This group includes only the lymphosarcomas and epitheliomas. The syndrome usually presented by these tumors is not generally recognized. Many of the patients are operated on and treated for months or years without a definite diagnosis, owing to the fact that often they have no nasal or nasopharyngeal symptoms.

Patients with cases of this type are sent to my section for examination from other sections because of some finding which suggests the nasopharyngeal syndrome. Seventy-four operations were performed on the seventy-nine patients for relief of symptoms before a diagnosis was made. Tonsils and adenoids were removed in twenty-four cases; the glands of the neck in eighteen; and wisdom teeth were extracted in twelve. Intranasal operations were performed in nineteen cases, which included ethmoid, antral and septum operations. Mastoid operation was performed in one case.

From the neurologic standpoint, the nasopharynx has been overlooked. As Dr. Woltman says, in nearly one third of the cases of malignant tumors of the nasopharynx, there are neurologic findings.

Dr. M. A. Bliss, St. Louis: Our experience with cases of this type has been largely in confusing them with the tic douloureux. Nearly all of the cases we have seen here have been diagnosed before coming to us as trifacial neuralgia.

Abstracts from Current Literature

DEMENZIA AFASICA (BIANCHI'S DISEASE): A CLINICAL STUDY.

ENRICO ROSSI, Ann. di nev. **1**:1, 1922.

The whole article might be summarized in the words of the author: "The hurried ultramodern conceptions (especially those of Marie and Head) of this subject have, instead of imperiling a magnificent structure, simply succeeded in constructing small buildings which are incapable of holding all the clinical pictures. Psychophysiology has succeeded in furnishing us with clear knowledge of the various speech centers, based on certain embryologic and developmental facts integrated with numerous accurate clinical and anatomic observations." The author gives credit to Bianchi for first accurately describing the mental side of the aphasic in 1887; that is, long before Pierre Marie did so.

The author reports a case of aphasic dementia in a 33-year old man who had previously been mentally normal. He became depressed by family worries, was suspicious, had lacunar memory defects and neglected his affairs. He was picked up in Milan disoriented and with signs of alcoholism. On examination, there was a generalized tremor of all extremities made worse by movement; uncertain and shuffling gait. He could not stand on one foot and was unable to obey simple commands, such as to button his coat, squeeze one's hand, etc., without great difficulty and much retardation. The right hand was weak. There was no facial weakness. The pupils were sluggish, equal in outline and size, and vision was equally diminished in both eyes.

Apparently there were sensory changes in the right hand. There was no Babinski sign or clonus; the patellars were hyperactive and equal. The patient was stupid; he appeared dazed and said nothing, even if directly addressed, unless the remarks were repeated several times; then he would say simple words, such as "mamma" or "Giuseppe." His name was pronounced Gius-pe. He had difficulty in repeating even monosyllables. He turned in the direction of sounds. He seemed to understand chiefly by signs and motions. He gave spontaneously a good account of happenings in his life prior to his illness, but chiefly by recalling visual imagery. He had poor verbal and visual images, but especially bad auditory ones. He was best able to recall visual images of events, objects and persons but could not translate these into words, even if they were suggested to him by asking him to copy or by dictating these things to him. He could not write his own name spontaneously. He read poorly and failed to copy even large letters. When asked "How old are you"? he would remain silent and apparently did not understand, but as the question was repeated he would write incorrectly with detached syllables and in a hesitating manner, repeating the request. If anything was dictated to him, the result as he wrote it was not understandable. Vowels and syllables were transposed.

The author explains the patient's difficulty by assuming defective formation of auditory, verbal and visual images and lack of coordination in the field of ideation of the formation of letters and syllables in the construction of speech. The patient's ability to write fairly correctly simple dictation after much repetition was due to integrity of the writing center and freedom of the centrifugal conduction pathway from it, and to a blocking of the pathway from the auditory word centers to the graphic center. This explanation of course does not tell

the whole story nor does it adequately explain any considerable part of the patient's trouble. He repeated, with omission of syllables, the names of objects shown him and calculated poorly even simple sums in addition and multiplication. His answers in writing were unintelligible hieroglyphics. He did recognize some colors but confused blue and black, yellow and green.

The patient was a dement. His ideas were necessarily confused, because of the fragmentary information he received. He was silly and euphoric. However, with verbal auditory reeducation he should improve. As he grew to recognize the sound of monosyllables, he was made to repeat them in words. As this improvement progressed, there occurred an improvement in copying and writing spontaneously, although still with a great percentage of error.

How the author arrived at his localization of the trouble in the temporal and inferior parietal lobes is hard to understand even though he points to the absence of hemiparesis (How explain the weakness in the right hand?) as removing the lesion from the third left frontal lobe, which he says is the site of lesions in paralytic aphasic patients. The patient therefore demonstrated as a result of these lesions: word deafness, alexia and agraphic, plus grave mental deterioration.

Bianchi, in 1921, differentiated the type of dementia in senility, dementia praecox and paresis from that which occurs in aphasia. In the former types the defect is global, affecting perception, association and memory and disturbing affect and attention. In aphasia, however, the rest of the cortex with the exception of that which has to do with language functions is intact. Is the aphasic demented simply because he is aphasic? The author argues the question. Language, intelligence and feeling develop apace as the individual makes contact with his environment. It is such an intimate evolutional synthesis that in breaking down the disturbances of language there are manifested disturbances in the production of vocal sounds and combination of syllables. This, of course, is the law of the beginning of destruction in disease of our most recently acquired functions.

Language and intellect are so intimately conjoined that the slightest disturbance of the former disturbs ideation in a particular manner much different from the disturbances seen in other mental conditions. In idiots and imbeciles the spoken word is either monosyllabic or extremely simple with much error of construction in phrasing, etc. In dements, however, speech is more of the confused type because of poor associations of words and ideas making concepts impossible and resulting often in perseveration of senseless syllables or phrases. In all of these cases one cannot speak of aphasia because, while the intelligence is severely disturbed, the use of language is not lost. Therefore, there is not an absolute connection between language and intelligence. Even in the sensory aphasias of Wernicke and the word deafness of Kussmaul, in which intelligence is so deeply disturbed, apparently the explanation is to be found in the fact that auditory images are so much more important than visual or motor images in building up concepts.

In the author's case the paraphasia, paragraphia, alexia and auditory amnesia made the synthesis of concepts impossible, thus explaining his dementia. He also had violent impulses (the patient was destructive and assaultive) which might lead one to believe him to be a real dement if it were not for the differential points already mentioned.

Thought is an intricate process requiring an exquisite harmony in the integration of various association cells in the cortex; only when thought is spoken is the voice necessary (speech). The word may be written or seen.

When one reads, one articulates mentally; therefore it follows that the articulate element in reading is of primary importance, the visual recognition being of secondary value. Or the word is revealed through the pressure of fingers on a pen in writing as occurs in the blind. In that case the tactile pressure sense is of secondary importance, internal speech causing the conversion by means of the pen into the written word.

In the author's patient the center for word images was not injured in its cellular (cortical) elements, but along the tract uniting in association the center for auditory memories and the psychomotor center of Broca, which explained the fact that he could in small part invest his ideas with the spoken word. The auditory word center is of great importance attracting to it the streams of association fibers from the kinesthetic, visual, gesture, touch and hand centers. Speech is possible, however, by the exclusive use of pathways from the visual, hearing, touch and movement centers directly with the prefrontal centers. But refined, elevated ideas and concepts can only be expressed when the cells presiding over the imagery of the spoken word are brought into play. This center is the Broca area and this conception has successfully withstood all attacks since 1863. Mingazzini has assigned to Broca's areas in both hemispheres the function of storing the motor images of language.

The author believes that the little used cells of the right Broca's area may, on occasion, assume the functions of the disturbed left area in cases of aphasia. He believes that the verbal auditory images are stored in the posterior third of the first left temporal lobe. In spite of the fact that his patient showed verbal auditory aphasia he was able to repeat, parrot like, names and phrases, though often incorrectly, just as a child does when it repeats without understanding the words it hears. There was incoordination between the movements necessary to articulate words and the motor articulate memories, also of the vision of the written word and incoordination between the motor writing memories and the written word. Probably words frequently repeated are actually registered in the auditory area as images of the sound of the spoken word. The child who hears is under the instinctive necessity to repeat because of the motor speech area. This, of course, places the author in the position of giving the child a speech area before it is able to speak or see and understand what it sees, or understand what it hears. It is practically the old facultative doctrine over again.

The author's patient not only had word deafness, but he did not recognize other sounds; therefore there existed a profound mental deficiency. Bianchi formulated the doctrine that the prefrontal lobes were the synthetizing centers directing and regulating the material elaborated by the sensory areas, and these later when dissociated were simply inadequate and weak, resulting in an appearance of dementia.

The author as a representative of Bianchi's school disagrees absolutely with Head. Bianchi has clearly shown that aphasic patients eventually, because of their defects, become demented. They remember nothing of what has happened to them, even recently; they lose the memory of objects, even though they understand what is said to them and are able to obey spoken commands. The author again attempts to classify his case; he says it was not one of pure word deafness nor of ordinary sensory aphasia, but a type of the transcortical aphasias of Lewandowsky. This case combined the elements of sensory aphasia and word deafness, because while he could hear he did not understand what he heard. He also had paraphasia—a conduction aphasia due to interruption of the auditory and motor pathways. No less important was the alexia

and paragraphia. This was due to a break in associations between the auditory word area and the visual, because writing is only possible through verbal association with the motor and visual areas. The depression in the word-acoustic area was felt also in the word motor and word visual areas making the recalling of images difficult.

The author calls attention to the hemiopically contracted visual field in his patient as proof that the visual pathways were involved rather than the word center itself. The patient also showed grave word memory defects causing a notable defect of intelligence even to dementia. For this reason the lesion is placed in a circumscribed area in the left temporal lobe and inferior parietal, also partly in the superior temporal gyrus in the insula and in the base of the ascending frontals (what real cortex was left whole?). One can best give the kind of reasoning employed by the author by simply doing as I have done—making practically a translation of the whole article. Its many discrepancies, its fallacious psychology are even more obvious in the original. All of the author's statements are based on a clinical case, neurologically incompletely examined. The diagnosis may even be questioned. Was it really a case of true aphasia even as clinically presented?

OSNATO, New York.

CONTRIBUTIONS TO THE STUDY OF SENSATION. H. DOEBELI, Schweizer Arch. f. Neurol. u. Psychiat. **9**:227-243, 1921.

The sensation of itching was studied by the application of an itching powder (mucuna pruriens). The subject was blindfolded and not told what was to be expected. By means of a skin microscope it was seen that this so-called powder is really not a powder at all, but that it is made up of numerous fine, needle-shaped hairs from 3 to 8 mm. in length and 0.25 mm. in thickness. These hairs have a dull and a sharp end and are quite rigid. On the slightest movement the sharp end imbeds itself in the corneal layer of the skin to a depth of less than 0.5 millimeter. In a normal subject the opposing surfaces of the fingers, the volar side of the forearms, especially near the wrist, the interscapular region and the tibial crest are most highly irritable, while the palms of the hands and the soles of the feet are least so. In addition to localization, the degree of itching produced is also dependent on the number of hairs applied. In the three cases of syringomyelia under investigation, the powder was applied in the form of streaks passing vertically and horizontally to the borders of the anesthetic areas.

An attempt was made to determine whether this itching was produced chemically or mechanically. Analysis showed that there are no acids or toxins present, such as Haberlandt found for the nettle. Other factors which speak for a mechanical basis of itching are the fact that triturated spun glass or a vibrating tuning fork produce this sensation, and that the itching can be stopped at once by removal of the powder with soap and water, which is not possible in nettle rash or insect bites. When a needle is pricked into the skin pain results. The difference, mechanically, between the production of pain and that of itching is that to produce the latter the stimulation must be minimal, and that no less than two or three pain endings must be stimulated simultaneously. It was found, in cases of syringomyelia, that wherever there is loss of pain sensibility, itching cannot be produced, even though tactile sensibility remains normal. Where pain sensibility is normal it is always easy to produce itching. While the difference in production of pain and itching seems to be only one

of degree, and the impulses presumably travel the same tracts in the cord, the affect reaction produced by these two types of stimulation is quite different and must be a function of the brain.

Pressure-pain sensibility was investigated by means of Head's instruments. It was found in the dissociated anesthetic areas of the syringomyelic patients under observation that pressure-pain sensibility was reduced. Up-to-date impairment of this form of sensibility was described only over the totally anesthetic areas (Schlesinger). There are cases of syringomyelia in which analgesia of deep structures coincides with analgesia of superficial structures; in such cases one is inclined to assume that these tracts ascend the cord in juxtaposition. In one of Doebeli's cases, however, there was complete superficial analgesia, while pressure pain was preserved. It is possible, therefore, that normal pressure pain is made up of two components, that is, pain caused by stimulation of deeper structures. Furthermore it appears that if pressure pain is normal while there is complete anesthesia of the skin, it must pass up another part of the cord.

Joint-pain sensibility was investigated by hyperextension and hyperflexion of the joint under consideration. This can easily be done with all joints working on the hinge principle. The examination is simple, the responses accurate and immediate. It was found that in syringomyelia joint pain may be diminished or lost. In the three cases under investigation, this form of pain sensibility was lost in all joints in a field of complete loss of superficial and pressure-pain sensibility.

Position of joint sensibility was tested in the usual manner by asking the patients to indicate any change of movement in the joint. The three patients examined gave normal responses. It demonstrated that this form of sensibility may be preserved even when joint pain sense is completely lost. Doebeli thinks, as do von Frey and Meyer, that postural sensibility does not belong to deep sensation, but is a quality of superficial sensibility produced by slight movements in the skin over the joint under consideration. In support of this he cites the experience of Vanghetti-Sauerbruch, who found that a patient having an artificial elbow with a normal stump above could detect the slightest movements of this elbow, presumably through the slight pressure and tension changes produced in the skin above.

Following the application of an Esmarch bandage a sensation of blood hunger appears; on its removal there is a sensation of blood passing through the vessels. Doebeli believes that these forms of sensation, while well understood in a general way, have not been described before. When an extremity has been emptied of blood there is a sensation of heaviness, weakness and fatigue. Syringomyelitic patients retain this form sensibility. The return of blood to the anemic extremity at first produces an unpleasant feeling, then a sensation of burning, and shortly a pleasant sensation of warmth. Although these patients lost temperature sensibility, they retained the burning and warmth which goes with this.

In order to test the ability of a patient to perceive the direction of rapidly succeeding stimuli, Doebeli stroked the skin in different directions with the tip of his finger. The result was interesting in that every variety of disturbance was noted. No definite rule could be established. In a general way, where there was diminished tactile and localizing ability, stroking of the skin was simply perceived as touch. Disturbances of directional sensibility in the main were present only where superficial sensation was involved; in one case, how-

ever, in which this was normal the patient was quite unable to indicate the direction of the stimuli over certain areas. This was verified repeatedly over a period of three months.

From the psychogalvanic investigation method M (Veraguth: Das psychogalvanische Reflexphänomen, Karger, 1911) was employed. The stimuli included acoustic tests, pricking of the skin in different regions and points de feu. The result was instructive in that there was no galvanic response wherever superficial sensibility prevented the appreciation of the stimulus. The writer recommends a wider use of this method in determining whether an anesthesia is of hysterical origin or not.

WOLTMAN, Rochester, Minn.

THE PHYSIOLOGY AND PATHOLOGY OF TICKLING. LUIGI INSABATO, Riv. di patol. nerve. e ment. **26**:121 (Nov. 12) 1921.

The author arrives at certain conclusions concerning the affective sensations of tickling and itching, based on the physiology of the condition as we know it through the work of many authors, whom he quotes, and also on certain original observations made on himself and on twenty-nine patients. These patients suffered from hemiplegia, with or without thalamic or other sensory disturbances, dementia praecox or manic depressive psychoses. There was a group also of perfectly normal persons.

In some of the cases of hemiplegia, with thalamic or other sensory disturbances, the loss of the normal tickling sensation was unilateral. Some patients having postencephalitic phenomena were also included in the twenty-nine subjects experimented on.

The author draws a very sharp distinction between the sensation of tickling, which he calls "Solletico profundo," and the sensation of itching, which he calls "Solletico superficiale."

The superficial sensation which he calls itching is characterized by the following special considerations: 1. It is produced by gently stroking small areas of skin or mucous membrane. 2. It may be produced by oneself. 3. It is strongly analogous with the spontaneous sensation of pruritis. It is also characterized by the fact that the sensation lasts a considerable time after the stimulus is removed, and only gradually disappears. It may, however, be made immediately to disappear by scratching or strongly rubbing the part stimulated, just as one obtains the sensation of satisfaction when a pruritic spot is scratched. The sensation is also further easily inhibited by the will.

This particular type of "Solletico" is very different from tickling, which is produced by the irregular and energetic stroking of certain parts of the body, namely, the axilla, the sides of the chest, the neck, the soles of the feet and the abdomen.

This tickling sensation cannot be self-provoked. It depends to a considerable extent on deep sensations and ends when the stimulus is removed. It is invariably tied up with motor reactions which have the characteristics of reflex acts. The author also feels that the superficial abdominal reflexes are intimately connected in their physiology with this latter sensation ("Solletico profundo"). This last affective sensation of tickling is very complex and depends on the special consciousness of a peculiar state of the organism, particularly the cutaneous and musculo-aponeurotic sensations.

There is also added the perception of reflex muscular movements of the regions stimulated and of other parts of the body remotely removed from the

point of stimulation. These reactions may be attitudes of mimicry or emotional attitudes of crying or laughter, and various evidences of changes in the sympathetic innervation may also make themselves manifest. These last may be vasomotor, secretory, respiratory or cardiac.

In other words, when the sensation of tickling is actively induced, one obtains a reaction which is really a profound emotional discharge obtained through reflex paths stimulated peripherally through the aponeurotic tendinous pathways, chiefly.

One, therefore, sees why the sensation of superficial "Solletico" (itching) cannot be the same as the great emotional discharge which accompanies tickling. The emotional element in the former is very slight, because the sensation can be self-induced. In other words, the affect element predominates in tickling or ticklishness, whereas the sensation element predominates in itching. Vasomotor and pilomotor reactions also occur in itching, but are only local sympathetic reactions.

The author states that while the phenomenon of ticklishness is an emotional reaction, it is a more primitive form of emotional reaction than one sees in fear, joy and pain. There the reaction is less a spastic one than it is a tonic contraction limited to the muscles of expression; whereas, in ticklishness, extensive muscular movements occur of a convulsive type, with uncontrollable laughter or crying. These last two states which accompany ticklishness help to explain the phylogenetic origin of the phenomenon.

The author thinks that the motor phenomena and ticklishness, namely, the rigidity of muscles close to the point of stimulation, opisthotonos, etc., show how closely allied it is to what occurs when the abdominal reflexes are obtained. Both of these are probably due to activity of the sympathetic nervous system through its connection with the motor extrapyramidal pathways in the basal ganglions.

Insaboto argues that the presence of painful ticklishness in certain of his cases showing psychic reactions and mental confusion and in certain of his postencephalitic cases with syndromes of the corpus striatum attests the importance of the basal ganglions in the production of this sensation. In further support of his theory that both the abdominal reflexes and ticklishness have a sympathetic basis, he calls attention to the fact that ticklishness has its point of strongest stimulation in the sides ("fianchi") where the most definite segmental sympathetic innervation also exists, supplying the large muscles of the abdomen.

Great stress is laid on the fact that some of his cases showed unilateral absence of ticklishness, and precisely in those cases was it true that the signs pointed definitely to lesions in the corpus striatum.

According to the principles of Vogt, the center for ticklishness, therefore, must exist in the neostriatum. This theory is based on the principle laid down by this investigator, who says that pallidal syndromes are always bilateral, while neostriatal syndromes are unilateral.

The author disagrees with Havelock Ellis that ticklishness is increased in the manic-depressive insanity. In two of his cases, it was diminished.

The author further feels strongly that his studies in connection with the pathology and physiology of ticklishness show that hysteria may have an organic basis in functional disturbance of the thalamus and basal ganglions. He specifically refers, however, to the motor crises of hysteria. In fact, he feels that the intense emotional crisis exhibited by the hysterical patient,

spontaneously, might be interpreted as a greatly exaggerated pathologic state of similar character as the normal emotional reaction, following active strong tickling.

He finally concludes that the significance of tickling is not teleologic but phylogenetic. In other words, tickling is an undifferentiated, general, non-specific emotional reaction, upon which has been gradually built the more specific utilizable colorings, namely, the emotional reactions brought out in defense, eroticism, play, fight, etc.

The article takes up forty-five pages of the number in which it appears and contains a splendid bibliography with many useful references. It is, furthermore, very well written. The only discrepancy which I found in the author's statements was his assertion, made several times, that the abdominal reflexes were like the reaction of tickling, in that they were not autoprovocable (p. 135). The morning after I had finished reading the article, I asked a psychoneurotic patient who was completely negative from the organic neurologic point of view to stroke his own abdomen and was able to see each one of the upper and lower abdominal reflexes come out quickly and actively.

OSNATO, New York.

FURTHER PATHOLOGICAL STUDIES IN DEMENTIA PRAECOX, ESPECIALLY IN RELATION TO THE INTERSTITIAL CELLS OF LEYDIG. FREDERICK W. MOTT and MIGUEL PRADOS Y SUCH, Dementia Praecox Studies, Psychiat. of Adolescence **5**: No. 2 (April) 1922.

Mott compares the histologic pictures of the testicular interstitial cells in the various psychoses with the normal picture at different age periods and with each other. Hematoxylin eosin and Heidenhain eosin technic were employed. Irreproachable normal material was examined at birth, at 4 months, at 10 years and after puberty. The study of tissue from young adults dying from shock convinced Mott that "Leydig cells have a comparatively short life and are continually maturing, decaying, and being renewed. All stages of small nuclei resulting from active division can be observed, followed by division of cell and growth to the mature cell, such as was seen in the newborn child. The cytoplasm of the normal mature cell is abundant and is stained by the eosin dye a deep pink, so that with a low power, islands, columns, and islets of cells can easily be recognized in the interstitial tissue.

When examined with an oil immersion details can be observed which cannot readily be seen with a low power; e. g., the amount of chromatin in the nucleus can be gauged and varying degrees of vacuolation in the cytoplasm corresponding lipoidal contents can be estimated. "I have come to the conclusion from my observations that vacuolation and disappearance of the pink cytoplasm are associated with a tendency to make the outline of the cells ragged or indistinct; and if marked, to convert the island of cells into a nucleated pale vacuolated syncytium." In slides from one of three octogenarians, while there was, of course, diminished spermatogenic action and considerable diminution in the number of interstitial cells, yet, they appeared fairly normal and presented less evidence if functional regression than did the majority of the cases of dementia praecox. Pigmentation is presumably a criterion of senility, yet, it was found in the majority of the group of schizophrenic patients who died before the age of 30. In twelve patients with paresis there was only one complete arrest of spermatogenesis. "Moreover, the nuclei and the mitotic figures showed a good basophil reaction, contrasting in this respect to the tubules in the earlier stages of dementia praecox where as often as not I found unequal

basophil nuclear staining." In manic-depressive conditions terminating in deterioration and in so-called "dementia presenilis" the findings were similar to those observed in advanced dementia praecox. In benign manic-depressive cases there was active spermatogenesis, but relatively deficient interstitial preservation. Twenty-seven cases of dementia praecox were included in the series. Here the results may be classified according to the severity of the regressive modifications. In the first stage "active spermatogensis could be observed in numbers of tubules, but examination with an oil immersion lens showed that the heads of the spermatozoa were not infrequently of irregular shape, unequal size and staining with eosin instead of the basic dye." In the second stage there were "many tubules showing active spermatogenesis, but many in which there was obvious regressive atrophy of the spermatogenic cells and thickening of basement membrane. There were pronounced changes of the Leydig cells in both." There were nine instances of pronounced spermatogenic regressive atrophy of tubules, and no eosin clumps of Leydig cells could be seen with low power. In the final stage were found "no spermatogenesis, tubules atrophied, often containing only Sertoli cells, with lipoid granules, thickened basement membrane. No normal Leydig cells—generally increase of fibroblasts."

Cause and effect conclusions are not justified by Mott's presentation and are not claimed by him, but he should be credited with a valuable contribution.

STRECKER, Philadelphia.

PATHOLOGY AND TREATMENT OF SPINAL CORD TUMORS. OSKAR FISCHER, Ztschr. f. d. ges. Neurol. u. Psychiat., No. 76: 81, 1922.

Fischer considers several points: treatment by means of the roentgen rays, the occurrence of tumor cells in the spinal fluid, the arrangement of the sensory tracts in the lateral columns and the significance of the abdominal reflexes.

He treated two patients with metastatic malignancy of the spine by means of the roentgen ray. In each case on the following day a trophic cutaneous disturbance developed rapidly and progressed to deep ulceration followed by sepsis which eventually caused death. The nervous symptoms were much exaggerated during the first two days, the partial paraplegia becoming complete, with retention of urine and complete loss of sensation in the area of previously disturbed sensation. Lumbar puncture showed a large increase in the number of cells, and those which before had appeared normal were now shrunken and vacuolated, stained poorly and otherwise appeared necrotic. After a few days, however, the power returned to some extent in the legs, and sensation was much improved. There were hyperesthesia and spontaneous pain in one of the cases.

In two other cases the effect of irradiation was gratifying. In both cases Fischer found in the fluid what he believed were tumor cells; yet he was unable to localize the level satisfactorily, and the distribution of the sensory disturbances made him diagnose intramedullary tumor. Here also irradiation was followed almost immediately by aggravation of symptoms of cord compression, but by no trophic disturbances. Also the number of cells in the spinal fluid was increased, and the large heavily stained cells had become pale and vacuolated. In a few days, however, the disturbance cleared up only to be repeated at each successive irradiation, but with gradual disappearance of

the signs and symptoms of tumor, even the spinal subarachnoid block, until the patients were discharged, one having recovered partially and the other completely.

Fischer recommends irradiation of spinal cord tumors when operation is contraindicated by a poor general condition, primary malignancy elsewhere in the body, when the level is uncertain and when tumor cells are found in the fluid. He argues that this last can take place only when a soft unencapsulated tumor involves the meninges. His technic for the discovery of these cells seems rational.

FREEMAN, Philadelphia.

THE FIELD DEFECTS PRODUCED BY TEMPORAL LOBE LESIONS.

HARVEY CUSHING, **Brain 44**:4, p. 341, 1921.

Cushing reports on fifty-nine brain neoplasms in which the temporal-sphenoidal region was implicated, with particular clinical and pathologic reference to quadrantic field defects. Accurate perimetric graphics were obtained in thirty-nine cases. In six there was no field hiatus; eight had already advanced to a homonymous hemianopsia; and in twenty-five there was more or less quadrantic defect. The latter group was divisible into the stationary type, the cases which were in the process of advancement to a homonymous hemianopsia and those in which the quadrant was a recession phenomena resulting from a reduction of pressure by means of decompression. As a clinical criterion of gross temporal pathology, one may quote Foster Kennedy's well known syndrome. "Common to a tumor of either lobe were: (1) convulsions of major and minor (uncinate) type, (2) bilateral choked disc, usually more marked on the side of the lesion, (3) post-epileptic transitory disturbances of motion and of the reflexes which later become persistent." In addition, a tumor on the left was said to produce some degree of aphasia. Cushing's analysis of his material which in general had not reached such an advanced pathologic stage constitutes a valuable extension of our clinical knowledge. Of primary importance are the quadrant defects. Generalized convulsions appeared in twenty of the fifty-nine patients, the greatest number in one person being twelve. While petit mal and dreamy states occurred in twenty-four instances, true uncinate seizures with characteristic olfactory or gustatory impression appeared only fourteen times. The tremendous importance of careful perimetric studies is proved by the fact that field defects were present in eighteen cases in which no history suggestive of petit mal or dreamy states could be secured. Visual hallucinations were recorded in thirteen cases and were almost always related to the uncinate seizures. Such hallucinations are pictorial as distinguished from the relatively simple visual phenomena (colors, lights, etc.) of occipital disease and "certainly bear some relation to the damaged geniculo-calcarine radiation, for in this series, whenever its situation has been mentioned, the hallucination has always been referred by the patient to the side opposite that occupied by the lesion, in other words, in the defective fields." One is somewhat surprised at the comparative insignificance of the clinical auditory phenomena. Hearing was unimpaired in thirty-eight instances; there was slight controlateral deafness in five and ipsolateral in two instaces; eleven patients had mild degrees of tinnitus. Aphasia is dismissed as a neighborhood sign. Unless the fields are carefully traced, a temporal growth may be mistakenly diagnosed as cerebellar, for nystagmus, dizziness, vertigo, primary suboccipital headache were relatively frequent and even definite ataxia and static instability were not wanting. Cushing regards the ophthalmoscope as

less important to the neurologist than the perimeter, and he has presented a clear-cut clinicopathologic argument which should stimulate the free employment of this instrument of precision.

STRECKER, Philadelphia.

CEREBRAL AND UNILATERAL FEVER. OSKAR FISCHER, Ztschr. f. d. ges. Neurol. u. Psychiat., No. 76: 131, 1922.

Fever is a fairly common accompaniment of tumors of the basal portions of the brain, and is also seen in some cases of insanity, especially in the agitated depressed cases. In the latter a dose of morphin will not only stop the agitation but will also control the fever. On the other hand, sudden stopping of morphin in drug addicts will be followed by fever, a sort of rebound by the cerebral center of control. Aseptic fever has also been noted in cases of paresis when probably the infectious process was progressing in the corpus striatum. Though the center for heat regulation is situated in the corpus striatum, it controls the contralateral portion of the body, as has been observed in a number of instances. Heat production, of course, is peripheral; and in several cases that Fischer studied, in which lesions of the basal ganglions on one side were present, the temperature of the opposite side of the body was higher than that of the side on which the lesion was present, and sometimes higher than the temperature as taken in the midline by mouth or by rectum. This was not the temperature of the skin, but taken in the axilla or between the fingers or toes, a true measurement of the internal temperature on the two sides. The farther removed from the head the temperature was taken, the greater the difference on the two sides, for in the nares and the external ears the temperature was practically the same on the two sides.

In one case of paresis, in which differences of temperature were noted on the two sides, there were clonic forced movements that much resembled hemichorea. It might be argued that the cause of the higher temperature was the muscular activity, but Fischer says that even the most intense muscular exertion is followed by only a minimal rise of temperature; hence the difference observed must be due to faulty action of the cerebral controlling center. In one case of encephalitis, rhythmic movements of one side were manifest, yet no fever resulted until a pressure sore became septic; then that same side of the body exceeded the other in temperature by several tenths of a degree Centigrade. Fischer concludes that the pyrogenic agent, the toxin, acted more strongly on the damaged center in the contralateral portion of the midbrain.

The article is well written and points the way for further observations. Fischer himself suggests that the mechanism of heat production and sweat secretion may be studied by direct microscopic observation of the cutaneous capillaries. Again, in some cases of cerebral insult without paralysis, difference of temperature on the two sides of the body may help to localize the lesion or differentiate apoplexy from other causes of coma.

FREEMAN, Philadelphia

SEQUELAE OF EPIDEMIC (LETHARGIC) ENCEPHALITIS. WILLIAM HOUSE, J. A. M. A. **79**:211 (July 15) 1922.

The author says that doubt has been expressed as to whether any patients with epidemic encephalitis ever fully recover because so many have been left with disagreeable sequelae. After deducting the fatal cases, probably one third of the patients are now well, though with rare exceptions convalescence was prolonged; and he was indeed fortunate who, having suffered from encepha-

litis, was quite well at the end of a year, though many resumed work in from three to six months. The remaining patients are still uncomfortable, many of them helpless, more in a condition of semi-invalidism which permits some activities, but robs life of much of its joy.

He divides these chronic cases into four groups: Group 1 is composed of those who in the acute stages exhibit myoclonic symptoms and who still suffer from muscular jerking and twitching, though in steadily decreasing severity. They also exhibit neurasthenic symptoms.

Group 2 is made up of those who exhibit definite psychoses; the most common characteristics of these were suggestive of dementia praecox.

Group 3 is composed of those who showed symptoms of neurasthenia or psychasthenia. This is the largest group of the four.

Group 4 comprises patients who exhibit signs of gross organic lesion of the brain or cord, which he divides into three sub-groups: (*a*) those with hemiparesis, (*b*) those showing symptoms depending on pontile or medullary lesions, (*c*) parkinsonian cases.

Among atypical sequelae he notes two patients who had marked glycosuria after the acute onset of the disease, and he attributes this phenomena to irritation of the fourth ventricle.

NIXON, Minneapolis.

PATHOGENESIS OF DISTURBANCES OF SLEEP FOLLOWING ENCEPHALITIS LETHARGICA. Z. BYCHOWSKI, Ztschr. f. d. ges Neurol. u. Psychiat., No. 76: 508, 1922.

Though disturbances of sleep are especially common in children, they occur with some frequency in adults, and seem to be linked with disturbances of motility; whether these two are related directly, Bychowski is unable to state. The insomnia enters the clinical picture after the acute stage of the disease has passed, at a time when the parkinsonian features are also likely to appear. The insomnia is characterized by restlessness, the assumption of curious attitudes and even forced movements such as those seen in chronic chorea. The subjects are martyrs to the condition. In some way the restlessness is dependent on the supine position, for many of the patients sleep better when propped up in a chair.

That the condition depends on disease of the basal ganglions, Bychowski believes to be shown not only by the pathologic findings, but also by a study of a wounded soldier who had a fragment of bone from the parietal region driven deep into the brain. He showed the same inability to maintain a single pose long enough to get to sleep. The author has encountered similar difficulties in severe cases of paralysis agitans.

He inclines to the belief that the hypophysis is diseased in these cases, first, from the anatomic juxtaposition of the basal ganglions, the infundibulum, third ventricle and hypophysis; second, from reported pathologic alterations in this gland in cases of encephalitis, from histologic studies of alterations in the glands in hibernating animals, and finally, from the affections of the pituitary gland leading to somnolence on the one hand and wakefulness on the other. He shows that other symptoms of pituitary dysfunction have arisen in a large number of cases of encephalitis. He believes that the inflammatory process which began in the brain stem and basal ganglions diffused slowly and invaded the infundibulum and hypophysis, possibly by way of the third ventricle.

The article is suggestive, but no consideration of the sleep mechanism is complete without due consideration of disease of the great ganglion for afferent

impressions, the thalamus. The author throughout has used "corpus striatum" to include the pallidum, nucleus caudatus and putamen. These, it is well known, are concerned with motion rather than sensation. The suggestions as to the hypophysis, however, are especially helpful.

FREEMAN, Philadelphia

RESULTS OF FIFTY DECOMPRESSIONS FOR EPILEPSY. VOLLAND, Ztschr. f. d. ges. Neurol. u. Psychiat., No. 74: 506, 1922.

About half of the cases of epilepsy resulted from trauma, but among these the results were not markedly better than among the others. The patients seem to have been selected at random, rather than with the idea of choosing those most fitted for the operation. There were some whose attacks had existed over a period of twenty years, and in many over ten. Hence, the proportion of definite improvement is perhaps lower than usual. Out of the mass, however, for each case is considered separately, Volland draws certain conclusions as to the indications for operation. He says that early operation is preferable in traumatic cases, including birth injuries, and also in encephalitis originating in the acute exanthems. A clean-cut aseptic wound of the cortex he says leaves little or no reactive inflammation and causes no subsequent irritation. He recommends excision of a portion of the cortex even though no abnormalities are found in the hyperexcitable area. Contraindications, Volland says, are: age over 40, syphilitic infection, toxic states and evidences of congenital malformation. If these conditions are not present, he advises a trial of the operative treatment in all cases in which medical, hygienic and dietary treatment has been unavailing. He says that the few patients who can be redeemed from the fate of continued convulsions with later psychic degeneration will make the operation worth while. There were four recoveries, fourteen improvements and one postoperative death in the series.

FREEMAN, Philadelphia.

MONGOLIAN IDIOCY IN A CHINESE BOY. I. HARRISON TUMPEER, J. A. M. A. **79**:14 (July 1) 1922.

Cases of mongolian idiocy that have been reported up to the present time have occurred in the Caucasian race. The case described by the author illustrates the fact that mongolian idiocy occurs in the Mongolian race and that the features of mongolian idiocy are not masked by those of the Mongolian race.

This case also confirms the recent finding in mongolian idiocy described by Timme, which consists of an excavation of the anterior clinoid process and presumably under the olivary process and the optic groove. The theory of exhaustion as an etiologic factor in mongolian idiocy is not borne out by this case, since there were normal children born before and after the patient. However, the father was 57 years old at the birth of the boy.

The fact that the basal metabolism rate was not significantly lowered confirms the view that the condition is not, primarily at least, a thyroid hypofunction and should not, therefore, be confounded with myxedema.

NIXON, Minneapolis.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, May 26, 1922

CHARLES H. FRAZIER, M.D., *President*

HEMIHYPERTONIA APOPLECTICA: REPORT OF A CASE. DR. A. M. ORNSTEEN.

There are three reasons for presenting this case: (1) Its resemblance to the hemihypertonia apoplectica described by von Bechterew; (2) the presence of signs of optic thalamus involvement, and (3) the presence of multiple areas of cerebral softening in a young person with resultant pseudobulbar palsy.

The illness began eight and one-half years ago when the patient was 26 years old. At that time she had been married four years, had had two normal deliveries and no miscarriages. After a rather restless night she awoke unable to speak; she appeared to be greatly agitated, and although she understood when spoken to and seemed to make an effort to reply, she would point to her mouth and frantically cry out, "ah-ah," the only sound she could emit. This symptom persists to date. About a month later, she suddenly became hemiplegic on the left side; whether or not consciousness was lost I am unable to determine. The paralysis must have been complete because she was bedridden for about two years, becoming greatly emaciated and developing large bedsores on the left buttock and other pressure points on the left side. She was unable to walk unaided in a satisfactory manner at the end of three years. There was left hemiplegia with motor aphasia in a right-handed person.

The condition remained unchanged for the next three or four years, when her facial expression became somewhat fixed with the mouth wide open and a silly smile; there was much drooling, and she began to shriek spasmodically with sudden outbursts of laughter; also ability to get around diminished until she again became bedridden a year ago. She now has urinary and fecal incontinence.

Examination: She shrieks and laughs spasmodically; any form of stimulus, such as asking her to close her eyes, will result in one of these outbursts. She is mute but seems to understand everything said to her, responding correctly with gestures of her head and right arm, although her reactions are greatly exaggerated. She has never been known to cry involuntarily. Memory and orientation are apparently well preserved. Attention and perception are good. Further investigation of her mental processes is impossible, with the exception of writing. It is distinctly agraphic, although occasionally a word can be recognized. She attempts to write from dictation but only her name is partly discernible.

The pupils are irregular, unequal and react poorly to both light and convergence, which may be partly due to the existing primary optic atrophy. Vision cannot be tested, but there is no evidence of gross defect in the fields. Ocular movements are well performed without nystagmus. Volitional power in the frontalis and orbicular palpebral muscles is good. In the orbicularis

oris volitional power is poor, the woman being unable to bring her lips together, or to retract the corners of the mouth, but in a spasmodic outburst the orbicularis oris is actively contracted. The tongue lies motionless in the floor of the mouth, and the patient is unable to move it in any direction. Eating and drinking are interfered with, the soft palate is slightly raised on volition, and she is unable forcibly to bring the jaws together.

The left arm is held extended, and to passive motion the resistance is great, but she is able to raise the arm quickly above the head without much sign of rigidity. The same difference is seen in the left leg, i. e., a much greater tonicity to passive than to voluntary motion. The fingers of the left hand are strongly flexed over the thumb by a spasm, not a contracture. This spasm may be seen to disappear allowing the fingers slowly to extend and occasionally to overextend through spasm of the extensors. The same alternation of spasm of the pronators and supinators of the arm may be seen. It is a slow mobile spasm. The toes, although held mostly in a flexor spasm, occasionally become involved in this mobile spasm. She is able to raise the left leg quickly from the bed; her left hand-grasp, although weaker than the right, is fair. In other words, she has not a hemiplegia, but a hemihypertonia with spasm. The reflexes on this side are exaggerated and a Babinski reflex is obtained. During active movements on the right side, the left arm shows some associated movements.

Voluntary movements and power in the right extremities are good; the movements, as stated in the foregoing, are very active and quick in response to a stimulus. The reflexes are exaggerated and a typical Babinski reflex is also present on this side.

The perception of touch and pain is preserved on the left side, but it is not as keen as on the right. Point discrimination and localization could not be tested for obvious reasons. Thermal sense appears to be normal. If a key be placed in her right hand, with eyes blindfolded, when asked if she recognizes it, she will nod her head in the affirmative and take the key between her fingers and turn her hand as if opening a lock. With the left hand she is unable to recognize the key. A left hemi-ataxia exists. Pressure of the musculature on the left side is more painful than on the right; whether or not she experiences the dysesthetic phenomena of thalamic disease it is impossible to determine. For many months she has complained of pain in the left side.

The underlying pathologic factors are probably bilateral interruptions in the cortical projection systems. A lesion in the right capsule extending into the thalamus and lenticular nucleus may be surmised in explanation of the left capsulothalamostriatal syndrome, namely, initial hemiplegia with regression, hemihypertonia with spasm and hemianesthesia for deep sensibility, associated with a disturbance of emotional tone. A bilateral involvement of the corticopontile fibers for the pseudobulbar symptoms, interruption of the frontothalamic and the thalamofrontal fibers (the anterior thalamic peduncle), loss of cortical inhibition of the primordial emotional reflexes with elevation of affective tone and instability of the emotions were present. The initial loss of speech, before the involvement of the muscles of articulation, must be looked on as the result of a lesion subcortical to the left operculum.

The lesions are probably thrombotic softenings of syphilitic origin. The blood Wassermann test is negative; the spinal fluid was not examined because of unsuccessful punctures. The cardiovascular and renal systems are normal.

Roettiger, in 1921, gave the following points, among others, as characteristic of hemihypertonia apoplectica: Cases follow apoplectic hemiplegia with regression of paralysis; no secondary contractures occur as in capsular lesions; passive movement increases the tonus, voluntary movement diminishes it; movements of the unaffected side are more energetic than usual, sometimes assuming the character of associated movements; frequently forced laughter occurs; occasionally tremor and athetosis and dysarthia are seen.

DISCUSSION

DR. C. K. MILLS: To my mind, the idea of tonicity being due to a withdrawal of inhibition is not correct. Tonicity and other tonectic phenomena are results of actual stimuli discharged from cortical or subcortical regions, these impulses being often markedly interfered with in their transmission, as when the pyramidal system is diseased. Cases such as reported by Dr. Ornsteen may be due to lenticulocapsular lesions.

DR. M. K. MEYERS: This patient was in my service at the Jewish Hospital. I regarded her as having a case of pseudobulbar palsy. I think that she was less emotional at that time. Never, to my knowledge, did she act in the exaggerated manner that she does tonight. She has deteriorated markedly since I saw her last, over a year ago.

A CASE OF TUMOR OF THE OCCIPITAL LOBE. DRS. L. J. HAMMOND and J. HENDRIE LLOYD.

Ferrier believed that the region of the angular gyrus was especially the cortical center for vision, but he claimed that a lesion here did not cause hemianopsia but complete amblyopia of the opposite eye, and possibly partial amblyopia of the eye of the side of the lesion. In order to obtain hemianopsia he thought that the occipital lobe must be impaired along with the angular gyrus. These experiments on monkeys, however, are open to the grave criticism that it is quite impossible to measure the visual fields in a monkey.

Attempts have been made to distinguish the macular fields, or fields for central vision, from the panoramic fields, or fields for wider peripheral vision. It has been asserted, for instance, that in lateral homonymous hemianopsia the blind half sometimes shows a small central area, or half-area in which vision is retained; this is the so-called macular area; and in double hemianopsia this small central area may, it is said, still be active. In other words, the patient is not completely blind. He goes peering about as though he were looking through a knot hole. Those who still follow Ferrier believe that the center for macular vision is in the angular gyrus, but others locate it in the cuneus, on the mesial aspect of the occipital lobe, and believe that the fields for panoramic vision surround it. The latter view is probably correct, for thus the macula, or center of the retina, is represented in the center of the visual cortex. Bramwell, some years ago, recorded a remarkable case of bilateral cortical blindness, of twenty-five years' duration, with preservation of a small macular field in each eye, in which necropsy revealed a small normal area in each cuneus, surrounded by an area of degeneration in each occipital lobe. This would seem to prove that the macula is represented in the cuneus, and that the center for panoramic vision surrounds the center for the macula. In the human subject we are dependent on pathologic lesions, and such lesions are often too gross, or not well enough demarcated, to furnish an exact localization. Such as they are, however, we must avail ourselves of them; therefore, we ought to record those cases as they arise.

In the present case there was right lateral homonymous hemianopsia, which was practically the only localizing symptom caused by a tumor which compressed the left occipital lobe. The patient was a single woman, aged 53, admitted to the service of Dr. Hammond, in February, 1922. About ten months previously she began to have pain in the occipital region. The pain was severe but intermittent, with vomiting, lasting for from two to four days. There were intermissions of two or three weeks. Vision gradually failed, until on admission she could not see to read but she could distinguish faces across the room. There was no paralysis of any limb or cranial nerve, no convulsions and no anesthesia. There was some vertigo, but no forced movements. The head was carried tilted to the right. The mind was rather sluggish, general health good.

Examination revealed right lateral homonymous hemianopsia. There were no visual hallucinations. The gait was unsteady; some dysmetria of the hands was noted. There was no anesthesia, but some astereognosis of the right hand. The pupils were equal, slightly dilated and responsive to light. The Wernicke pupillary sign was lacking; that is, the pupils reacted to light thrown on the blind halves. There was no aphasia. Dr. Moore found choked disks of a high grade, small central vessels, edematous retinas, but no hemorrhages.

The roentgen-ray report was negative, as were the laboratory tests of the blood and spinal fluid.

The Bárány tests showed a lesion in the right hemisphere of the cerebellum, at or about the semilunar lobe. This localization did not agree with the one indicated by the other findings, but unfortunately it was allowed to determine the site of the operation. Dr. Hammond performed an operation over the cerebellum, but found nothing. The patient died about four weeks later.

The tumor was comparatively large, and sprang from the membranes of the left occipital lobe. It lay partly at the extreme posterior end of the lobe in such a way as to cause pressure on the mesial aspect of the lobe and on the cuneus or calcarine region. Hence it had rather unusual value as a localizing lesion. The injury done was almost entirely to the occipital lobe, although the size of the growth was such that it may have made some pressure forward on the superior parietal lobule. The temporal lobe did not seem to be involved.

The main features in this case were: severe headaches, paroxysmal in kind, with nausea and vomiting; papilledema, advancing rapidly to blindness; right hemianopsia; slight astereognosis of the right hand; unsteady gait, not forced or suggestive of cerebellar lesion.

The symptomatology is significant for what it includes and for what it lacks. There was no paralysis, no anesthesia, except the slight astereognosis; no convulsions; no affection of gait or forced movements, except an unsteady gait, partly due no doubt to increasing blindness; no aphasia. Of the positive symptoms the hemianopsia was by far the most significant, the only one that had any localizing value, except the astereognosis, which tended rather to indicate a possible parieto-occipital lesion and hence was a little misleading.

Affections of the form fields were seen, of course, in other than strictly localized occipital lesions. In another case a large tumor in the parieto-occipital region caused hemianopsia to the opposite side, but there were other symptoms that served to distinguish it. Cushing has recently called attention to tumors of the temporal lobe as causes of various types of anopsia. It is easy, of course, to understand that a lesion anywhere in the course of the optic radiations will cause such symptoms; but the point to be emphasized in

the present case is the fact that the lateral homonymous hemianopsia was the only reliable symptom, and that if we had relied on it we should have been led to the seat of the tumor.

We feel obliged to point out that in this case the Bárány tests were misleading. These tests are only tests of the vestibular nerve; the possibility of a misinterpretation of them is incalculable; and the doubt raised by them may be little less than demoralizing to the diagnostician. Why do we attach so great importance to this one nerve? We do not attach localizing value to a mere choked disk. Disturbance of the vestibular nerve, taken by itself, may be no more of a sure guide than a choked disk.

DISCUSSION

Dr. C. K. Mills: The one doubt that might have arisen in Dr. Lloyd's case was whether the lesion was on the surface or in the interior of the occipital lobe. The astereognosis is easily explained by the pressure or direct involvement of a part of the parietal lobe.

To a certain extent I am a believer in Bárány tests, as clear results can be obtained by this method in cerebellopontile angle lesions. Even an alleged Bárány determination of a cerebellar lobe lesion can be carefully scrutinized. The examination of panoramic and macular vision is important, as the former can be present without the latter or the latter without the former.

Dr. H. Maxwell Langdon: I feel that the Bárány tests are a valuable addition to our methods of brain localization; they are additional evidence, and should be weighed in the same scales with the other evidence. I know of some cases in which the Bárány tests have been almost astounding in the directness of their evidence, and other instances in which their findings did not fit in with other examinations at all. If we could distinguish between direct and transmitted pressure signs, many of our cases could be localized, whereas now we miss them.

When there is exact lateral homonymous hemianopsia, I believe that in ninety-nine cases out of a hundred there is direct and not transferred pressure.

Dr. J. Hendrie Lloyd (closing): I agree that the Bárány tests are of value sometimes in localizing peripheral nerve lesions and pontile angle lesions. In syphilis of the eighth nerve they may show that the functions of the vestibular nerve are abolished, and thus confirm the diagnosis of a lesion of the eighth nerve. But when these examiners get inside the brain stem they are lost. In one case of syphilis of the eighth nerve, the man who made the Bárány tests tried to draw conclusions as to localizations inside the pons. I did not agree with him. Inside the brain stem the course of the vestibular and acoustic nerves cannot be followed with scientific accuracy. When the attempt is made to diagnose a lesion in the right cerebellar hemisphere on data given by the Bárány tests, it is making deductions from insufficient premises.

Dr. Fay, I think, referred to hemianopsia in pituitary tumors. I think they are usually cases of bitemporal hemianopsia due to pressure on the chiasm. That is what is generally taught. I have not seen many such cases.

The question was raised as to the possibility of a lesion of the cerebellar hemisphere causing pressure upward through the tentorium and thus causing hemianopsia. I feel that the case is added proof that the visual cortex is on the mesial aspect of the occipital lobe. I do not believe that macular and panoramic vision are located in different regions of the cortex but that macular vision is localized in the cuneus and panoramic vision surrounds it.

MARKED ATROPHY IN EARLY TABES. Dr. Herbert Fossey.

The patient, a white man, 30 years old, was admitted to the Philadelphia Hospital Aug. 23, 1921, complaining of urinary incontinence and gastric pains. He presented marked emaciation and appeared to be very sick. Examination revealed severe cystitis, pyelitis and an infected penis due to continuous friction of the urinal in addition to the typical signs of tabes dorsalis. He was suffering intensely from gastric crises which had been present for the last six weeks. Two weeks prior to entrance he had been operated on for appendicitis.

The most striking finding was the extreme atrophy in the disease which was of only four years' duration. That his symptoms started one year after the initial lesion is noteworthy.

Déjerine mentions the tabetic type of neuritic atrophy which may be confused with tabes. Lapinsky speaks of an initial neuritis in young people which gives marked early muscular atrophy. According to Marie, tabetic muscular atrophies may be divided into two groups: (1) those appearing late, presenting a symmetrical distribution, rarely marked by fibrillary twitchings; (2) those occurring often in the earlier stages of the disease, usually unilateral in distribution, marked by fibrillary contractions and sometimes by the reaction of degeneration. The first group embraces atrophies confined to the distal portions of the extremities, and recalls the conditions found in multiple neuritis. The second group contains lingual hemiatrophy, localized atrophies of the shoulder, of the back, of the hand, and one-sided involvement of the cranial nerves. They are analogous to lesions of the gray matter. Both the central and peripheral lesions are found, and in the associations indicated in the foregoing. The wasted muscles present the usual histologic change due to degeneration in the lower motor neuron.

Herman Lippman ("Concerning Muscular Atrophy in Tabes Dorsalis") states that "Lapinsky and others have found that section of the posterior root causes changes in the cells of Clarke's column and in the nerve cells of the anterior horn; changes which in their essentials consist of a swelling of the cells and loss of Nissl bodies. From this standpoint he explains the atrophy in tabes. Déjerine thinks that the muscular atrophy of tabes depends on a peripheral neuritis, proceeding slowly to the anterior roots. The muscles which these nerves supply have thin round fibers which in portions fall apart and are filled with pigment. The connective tissues in these muscles are increased and rich in nuclei, the fibers thin and few. Clinically there is fairly symmetrical atrophy of the extremities. Fibrillary twitchings are not observed; the reaction of degeneration is frequently seen. Déjerine is of the opinion, because of these findings, that the spirochete or its toxin at times locates in the peripheral motor nerves. The clinical and pathologic findings are the same whether the neuritis is due to poisoning or to a mechanical injury. It has been known for a long time that in tabes, as in alcoholism, the motor nerves are vulnerable. A toxin which a normal person can withstand may injure the nerves of an alcoholic or a tabetic person. Leyden, Remark, Möbius and others believe that in tabes there is a tendency to paralysis because, owing to the degeneration of the posterior roots, impulses do not reach the anterior horn cells. The resistance of these cells is decreased, and they are easily injured.

An objection to the theory of Déjerine is that in his studies he used the older methods of staining, and the author believes that the newer methods, especially the special cell stains, are necessary to determine the entire picture, especially as regards the anterior horn cells.

The author concludes that muscle atrophy in tabes occurs under these conditions: (1) due to accompanying disease; (2) as a result of the general weakness and anesthesia of the muscles toward the end of tabes; (3) as a result of the peripheral neuritis brought out, not through the poison of tabes, but through other injurious processes; (4) as a result of the localization of the toxin of syphilis in the nerve roots and anterior horn cells, whereby the motor impulses are more or less impaired.

The spinal cord of the patient under discussion revealed the following: The usual degeneration of the posterior roots seen in tabes is very intense in the lumbar region and even in the midcervical region. The nerve cells of the anterior horns of the lumbar region show considerable degeneration of the type of central chromatolysis; that is, a disintegration of the chromatophilic elements, particularly of the center of the cell body with peripheral displacement of the nucleus. This is a common finding in multiple neuritis and would indicate that the peripheral nerves were considerably degenerated. The nerve cells of the anterior horns of the midcervical region show a similar reaction at a distance but not so intense. The nerve cells are possibly not so numerous as one would expect. Intense degeneration of the posterior root from the upper limbs with some central chromatolysis of the nerve cells of the anterior horns indicate that a similar degeneration of the peripheral nerves was present in the upper limbs. Such widespread degeneration of the posterior roots is uncommon in tabes of such short duration and the process had reached a height which is usually seen in tabes only after much longer duration. The action of the spirochete in this case must have been exceptionally virulent, producing within a short time lesions uncommon at so early a period.

DISCUSSION

Dr. C. M. Byrnes: I should like to ask Dr. Fossey whether there were any objective sensory changes in his case, and whether the patient had been treated with mercury or arsphenamin before the development of the atrophy. Through the courtesy of Dr. Spiller, I have been studying round cell infiltration in various nervous lesions and I was much interested to find that in syphilitic cords there is not infrequently, contrary to the usual teaching, marked cellular exudate about the anterior roots. In several instances, the anterior roots on both sides were practically embedded in a plastic exudate, sufficient, it seemed, to account for the occasional atrophies occurring in tabes.

Dr. Herbert Fossey: The patient had hyperesthesia generally distributed over the extremities. He had received no antisyphilitic treatment prior to his admission.

A CASE OF PERMANENT QUADRANT ANOPSIA, POSSIBLY DUE TO MIGRAINE. Dr. J. C. Mulrenan.

John F., aged 28 years, married, complained of defective vision. In 1918 he had had influenza and pneumonia. For several years he had suffered from periodical headaches; otherwise he has been well. His habits have always been good. The headaches occur about once in two weeks and are usually located in the right frontolateral region. During the attack he is pale, but as a rule does not vomit. There have never been hallucinations of vision, taste or smell. One evening in April, 1920, he had a severe headache. The next morning while quietly standing after some heavy lifting, he was suddenly seized with a "feel-

ing of numbness and pins and needles in the left hand, arm and side of the face. Everything became black, but he was not unconscious and did not fall." Immediately afterward there was a violent headache, and he vomited. For about five minutes he was completely blind. After the vomiting vision returned but was blurred, and it has remained so since.

Dr. L. C. Peter reported a refractive error (hyperopia) and left superior quadrant anopsia and a large scotoma for colors in the lower nasal area of the right field. Color fields were concentrically contracted following the form fields. An enlarged blind spot was present in the right eye, otherwise the eyes were normal. Neurologic examination was negative, as was also the medical report made by Dr. G. M. Piersol. Examination of the nasopharynx by Dr. Butler was also negative, with the exception of chronic pharyngitis. Syphilis was denied, and the Wassermann test was negative.

His mother and grandmother had suffered from similar headaches.

DISCUSSION

Dr. Charles S. Potts: This patient was in my service at the Polyclinic Hospital. While I at first thought that the attack was probably embolic, and a case somewhat like those described by Dr. Woods in the February number of the *Journal of Nervous and Mental Diseases,* the history of headaches, the fact that the mother and grandmother were subject to headaches of a migrainous type, the negative Wassermann test and the absence of cause for an apoplectic disturbance, made me think that this case bore a similarity to the cases described by Hunt and others occurring in patients subject to migraine.

Dr. C. K. Mills: I think it is a mistake to give out the idea that migraine can in some inscrutable way cause a more or less permanent anopsia or hemianopsia, unless a destructive focal lesion is present.

Dr. C. S. Potts: With reference to what Dr. Mills has said I would state that my belief is that arterial spasm caused the condition. Whether the spasm lasted long enough to cause degeneration, or whether thrombosis occurred in the artery, I cannot say. During an attack of migraine I believe there is arterial spasm, and it therefore might produce the contraction of the arteries that caused the lesion producing this condition. There is no reason to believe that the patient had syphilis; and he was carefully studied from all standpoints and no cause found for an embolism.

Dr. Alfred Gordon: We are accustomed to believe that migraine is a temporary but periodic condition, which comes and goes; but this patient had distinct subjective sensory phenomena, limited to the left arm. He had tingling in that arm and right hemianopsia. It is difficult for me to understand that migraine could cause a lesion of such character. I would attempt to localize the lesion in the posterior portion of the internal capsule and in the optic radiations. This would explain the hemianopsia and the sensory phenomena. I believe that the lesion is vascular. An alternating spasmodic contraction of the blood vessels is a plausible assumption.

Dr. H. Maxwell Langdon: There is a type of case which ophthalmologists see rather infrequently which may throw some light on what happens to the cerebral circulation in these cases of migraine; namely, spasm of the retinal arteries. Some years ago I reported such a case before the American Ophthalmological Society. It was that of a man who for many years had had attacks of transient monocular blindness, the attacks never being simultaneously bilateral—each eye was affected at different times; the attacks would last from three to five

minutes, during which time vision was completely gone, and then it would return to normal. Unfortunately there was no opportunity to examine the eyes during an attack. One eye eventually suffered from an attack which was permanent, there being a complete collapse of the retinal circulation. The man had advanced arteriosclerosis, and one of the interesting questions to be solved is whether spasm of perfectly normal vessels occurs. Should a spasm occur in normal vessels I do not believe it is as likely to be permanent in its results as when the vessels are sclerosed and are likely to become permanently blocked. Similar cases have been reported when examination was made during an attack, one case in this city being seen by several observers, among them Drs. Zentmayer and de Schweinitz. During the attack the retinal circulation would be completely lost, and then the vessels would gradually fill again until the condition was restored to normal. I think what happened in these cases is what happened in Dr. Mulrenan's case, only that in his case it happened in the cerebral circulation instead of in the ophthalmic.

Dr. L. C. Peter: Four or five years ago I saw a case similar to this one. It occurred in a young lawyer who had been over-worked, and who, in the midst of a conversation with his partner, suddenly became aphasic. He did not fall, but was hardly able to stand up. He had left-sided motor and sensory disturbances, which cleared up in a few days. On the day after the attack, he had a left inferior quadrant anopsia which changed slightly in the course of five or six months and finally left quite a defect in this particular area. He did not have a lesion in the cuneiform body, but a lesion somewhere around the capsule, possibly in the beginning of the optic radiation. The condition cleared up entirely, the aphasic phenomena lasting two or three days.

These fields bring to mind a thought of Dr. Cushing, when he referred to the asymmetry in homonymous hemianopsia, the greatest advance, as a rule, being homolateral to the lesion. It has been difficult for me to reconcile the cause usually assigned to this asymmetry with the facts in hand. Associated nerve fibers representing corresponding retinal points may or may not be in close contact after they leave the chiasm, during their course to the occipital lobe. Defective technic may lead to error and apparent asymmetry. The main factor, however, in asymmetry of homonymous hemianopsia is the relative difference of retinal sensitivity in the nasal and temporal retinae.

In the case of Dr. Mulrenan it is not likely that the lesion was in the cuneiform body, because of the motor and sensory symptoms, but far forward, probably in the beginning of the optic radiation of Gratiolet.

TUBEROUS SCLEROSIS. Dr. W. Freeman.

This paper will be published in full in a future issue.

DISCUSSION

Dr. N. S. Yawger: I have had three epileptic patients in whom I have made the diagnosis of tuberous sclerosis. Dr. Freeman has referred to two of these.

TWO CASES OF IDENTICAL ACHONDROPLASIA WITH EPICANTHUS IN BROTHERS. Dr. A. E. Taft.

Two boys, aged 16 and 9 years, respectively, showed identical anomalies, which were congenital and not progressive. The personal and family histories were negative; the Wassermann test was negative.

Both cases presented the following features: A lock of white hair at the midline of the frontal hair margin; bilateral epincanthus; narrow, high-arched palate with overlapping teeth; complete deafness; "high shoulders"—scapulae in embryonal position opposite lower cervical vertebrae; maldevelopment of elbow joints preventing normal flexion of forearms; radius relatively longer than ulna and maldevelopment of carpals, thus forcing hands into ulnar position; marked lack of muscular development of upper extremities reducing function to a minimum, though other skeletal muscles were well developed Intelligence was normal.

Book Review

PSYCHOANALYSIS. ITS THEORIES AND PRACTICAL APPLICATION. By A. A. Brill, Ph.B., M.D., Lecturer on Psychoanalysis and Abnormal Psychology, New York University. Third edition. Cloth. Price, $5 net. Pp. 468. Philadelphia: W. B. Saunders Company, 1922.

The fact that this book is now reprinted in its third edition inside of ten years speaks both for its popularity and for the growing interest in the subject. Shortly after the war, we witnessed a rapid increase in popular interest in psychanalysis, and on this wave of interest there floated to us a mass of books and magazine articles, some of them valuable but many little short of objectionable to the psychiatrist. Many medical theories and practices have had to withstand a similar flare of notoriety, and have done so. Now, with the newspaper popularity of the endocrins, it seems that psychanalysis may be suffered to drop out of the limelight to the sphere in which it belongs, as a part of medical practice. Psychanalysis was developed by a physician as a means of treating disease, and in medical practice it will always find its greatest usefulness. This book is written by a physician for physicians to tell them something about a method of treatment.

The author approaches his subject from a strict freudian point of view, with some references to the work of Jung and Bleuler. He makes no mention of the broader biologic principles which the English school have brought into the subject, where other instincts than the sexual are considered. The author's frankness of diction might offend the fastidious, but when writing about the psychology of sex one must use well-known terms which are not pretty, or euphemisms which easily lead to inaccuracies. The author is never guilty of the latter fault.

The book opens with a chapter on the psychoneuroses which presents Freud's views quite clearly. The following chapters on the psychopathology of every-day life, dreams and the actual neurosis, cover ground already covered in earlier editions. Masturbation forms the subject of the first new chapter. This chapter is more readable than many of the others and presents a fair, clear-minded view of this subject, still bound up with so much supposition and stupidity in many minds. The medical world needs more of such material and advice as this chapter holds.

The compulsion neuroses, the unconscious, the use of psychanalysis in the psychoses, and paranoia are treated in separate chapters, from the point of view that Freud has offered us. The new chapter on paraphrenia strikes one as rather unconvincing and leaves one with a doubt about its existence as a clinical state. In the third new chapter, homosexuality is presented with the author's characteristic frankness, and is well done.

The chapter on hysterical fancies and dream states contains much interesting material, and is one of the best in the book. The much discussed Oedipus complex gets a chapter to itself and shares with the following chapter on the only child, the quality of containing much good advice to parents which has little chance of being accepted in modern life in our large cities. Fairy tales and anal eroticism are treated in separate chapters, and the book closes with a long exposition of Freud's theory of wit, which is already well known

to psychiatrists. Appended to the book is a glossary which is quite incomplete, and one feels that the author has not been fortunate in some of his definitions.

On the whole, the book leaves a favorable impression. The arrangement of chapters is not good and there seems to be little system in the presentation of the subject. However, if one looks on it not so much as an exposition of psychanalysis as an exposition of the author's large experience with psychanalysis in the treatment of neurotic and psychotic patients, the book is distinctly of value. The captious critic will discover much in it with which he may find fault, but he who reads it for what it is—a medical presentation of a medical subject based on years of experience with patients— will glean from it points of view and hints of symptom meaning that will help him in the understanding and treatment of this largest and most neglected group of patients in practice.